Epilepsy & Spells

Seizures & other causes of Transient Neurological Symptoms

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Overview

- Differential diagnosis of episodic neurologic symptoms
- Epilepsy
  - Syndrome definitions
  - Types of seizures
  - Diagnosis
  - Therapy
  - Special populations

Differential Diagnosis for Episodic neurologic symptoms

- Seizure
- Syncope
- Cerebral ischemia (TIA)
- Migraine
- Sleep disorders
- Transient Global Amnesia
- Conversion disorder
- Malingering

Syncope

- Loss of consciousness caused by cerebral hypoperfusion
  - Cardiac arrhythmia
  - Orthostasis
  - Dysautonomia
  - Cough, urination, defecation
- Much more common than epilepsy
- Convulsions may be present in up to 50%

New onset sudden loss of consciousness with loss of muscle tone in adulthood is syncope unless proven otherwise

TIA

- Usually negative symptoms
  - Exceptions, e.g. limb shaking TIA
- Last minutes to an hour
- Not as likely as seizures to be stereotyped or recurrent

Sleep Disorders

- Hypersomnolence
- Hypnagogic/Hypnapompic jerk
- REM behavior disorder
  - May be presenting sign of PD or LBD
- Cataplexy
- Periodic limb movements of sleep
- Night terrors

Migraine

- Transient, episodic, and stereotyped
- May involve neurologic symptoms (aura)
- Neurologic symptoms develop over minutes
  - seizures, usually over seconds
- Aura precedes headache

TGA

- Sudden onset
- Duration typically 6 to 24 hours
- Memory impairment and confusion
  - May ask same question repetitively
- Usually able to carry on usual ADLs
- Resolves completely but no memory of events
- Up to 25% recurrence rate

Psychogenic non-epileptic spells (PNES)

- Typical characteristics
  - Eyes closed
  - Side to side head movements
  - Bilateral motor involvement with preserved responsiveness
  - Pelvic thrusting
  - Back arching
  - Prolonged screaming or crying

Features favoring seizure

- Preceded by aura
- Occurring out of sleep
- Duration 30 to 120 seconds
- Eyes open
- Postictal confusion
- Amnesia
- Injury (lateral tongue and cheek biting)

EPILEPSY Definitions

- Generalized vs. Localization-related
- Symptomatic vs. Idiopathic
- Symptomatic vs. Cryptogenic

Types of Seizures

- Simple partial
- Complex partial
- Secondarily generalized

- Absence
- Tonic-clonic
- Myoclonic
- Atonic

Simple Partial

- Focal neurologic dysfunction
- Without impairment of consciousness
- Usually "positive" symptoms
  - i.e. jerking/stiffening as opposed to weakness or tingling as opposed to numbness

Simple partial seizures

- Motor – tonic / clonic
- Sensory – paresthesias / buzzing
- Special sensory - olfactory / oustatory / auditory / visual
- Psychic - Déjà vu, depersonalization, micropsia/macropsia
- Emotional – pleasure / fear / anger

Complex Partial

- Focal neurologic dysfunction
- With impairment of consciousness
- May have similar signs/symptoms as SPS
- May display automatic behaviors
  - Lip smacking
  - Repeated swallowing
  - Manual automatisms, i.e. fidgeting, rubbing, picking, scratching

Secondarily Generalized

- May occur with or without a recognized preceding SPS or CPS
- Head and eye deviation may indicate [contralateral] hemisphere of onset

Generalized from onset seizures

- Absence
- Tonic-clonic
- Myoclonic

- Tonic
- Atonic

Absence Seizures

- Most commonly appear in childhood and resolve in adolescence
- Rarely presents in adulthood
- May persist into adulthood as part of JME or JAE

Absence

- Sudden onset behavioral arrest, unresponsiveness
- Typically less than 10 – 15 seconds
- Little or no postictal confusion
- May occur dozens of times in a day
- Can be made worse by sodium channel modulators such as CBZ, PHT, OXC

Myoclonic Seizures

- Brief and shock-like
- Typically involve limbs but may involve torso or head
- Tendency to occur upon awakening
- May occur singly or in brief trains

Other uncommon seizure types

- Myoclonic
  - Generalized epilepsy phenomenon
  - Tend to occur close to sleep onset or upon awakening
- Tonic / Atonic (Drop attack)
  - Seen in Lennox-Gastaut and symptomatic generalized epilepsy syndromes
  - Very uncommon in adult-onset epilepsy

Seizure Therapy

Seizure Treatments

- Anticonvulsant medication
- Implantable devices
  - Vagal nerve stimulation
  - Responsive neurostimulation
  - Deep brain (thalamic) stimulation
- Epilepsy surgery
  - Resection
  - Radiosurgery

Older Anticonvulsants

- Phenobarbital
- Primidone
- Phenytoin
- Valproic acid *
- Carbamazepine
- Clonazepam

2nd Generation Anticonvulsants

- Gabapentin
- Felbamate
- Lamotrigine *
- Topiramate *
- Levetiracetam *
- Zonisamide *
- Oxcarbazepine
- Pregabalin
- Lacosamide
- Clobazam*
- Tiagabine

Anticipated Anticonvulsants

- Brivaracetam
  - Chemically related to but more potent than levetiracetam
- Eslicarbazepine
  - Active metabolite of oxcarbazepine

Phenobarbital/Primidone

- M.o.A. - enhancement of GABA-A
- [+]
  - Effective
  - inexpensive
  - can be taken QD
- [-]
  - side effects – sedation, mood, bones, liver
  - drug interactions

Phenytoin (Dilantin)

- M.o.A. – inhibition of VG Na channels
- [+]
  - effective
  - inexpensive
  - can be taken QD (Dilantin)
- [-]
  - non-linear kinetics
  - side effects (ataxia, gingival hyperplasia, PN)
  - drug interactions (p450 inducer)

Carbamazepine (Tegretol, Carbatrol)

- M.o.A. – mainly inhibits VG Na channel
- [+]
  - Effective
  - Inexpensive
  - Well-tolerated
- [-]
  - Rare bone marrow or hepatic toxicity
  - 3rd leading cause of Steven-Johnson
    - HLA- B 1502 8% of Han Chinese
  - Drug interactions (p450 inducer)

Valproate (Depakote)

- M.o.A. – mainly GABA-A modulation, also affects Ca and K conduction
- [+]
  - Broad Spectrum
  - Non-sedating
  - Available in QD preparation
- [-]
  - Weight gain
  - Potential for hepatotoxicity
  - Hirsuitism, PCOS, teratogenicity

Gabapentin (Neurontin)

- M.o.A. - ? – VG Ca Channel modulation
- [+]
  - Favorable side effect profile, some beneficial
  - Renal clearance, no drug interactions
  - Little toxicity
- [-]
  - Low efficacy (except in elderly)
  - TID dosing

Lamotrigine (Lamictal)

- M.o.A. –VG Na Channel inhib, N-type Ca Channel modulation
- [+]
  - Very favorable side effect profile, some beneficial
  - Broad spectrum
- [-]
  - Rash, potential for S.J. synd, slow titration
  - Tremor, headache, insomnia

Topiramate (Topamax)

- M.o.A. – VG Na, GABA, AMPA, Ca, etc.
- [+]
  - Highly effective
  - Weight loss
  - Mood stabilizing, migraine preventive
- [-]
  - *Cognitive side effects
  - May cause renal stones
  - Weight loss

Levetiracetam (Keppra)

- M.o.A. – binds SV2A synaptic vesicle protein
- [+]
  - Broad spectrum, effective
  - Renal clearance, no drug interactions
  - Safe
- [-]
  - Mood and behavioral changes

Treatment of epilepsy in women

- Must take into account additional factors
  - Menstrual cycle
  - Contraception
  - Potential for pregnancy/teratogenicity
  - Reduced drug levels during pregnancy
  - Cosmetic effects of anticonvulsants
  - Special attention to bone health

Menstrual cycle and seizures

- Estrogen – pro-convulsant
- Progesterone – anti-convulsant
- Treatment of catamenial epilepsy
  - Increase AED during at risk period
  - Add BZD during at risk period
  - OCP
  - Progesterone IM depot

Contraception

- Estrogen and progesterone metabolized by p450
- Several AEDs decrease effectiveness of OCP
- Higher dose OCPs may be more effective
- Depot progesterone or IUD recommended

- OCP may reduce LMT levels

Pregnancy - counseling

- Risk of birth defects increased 2x in WWE
- All AEDs potentially teratogenic
- Seizures during pregnancy also hazardous
- Planned better than unplanned
  - Seizure free 1 year before pregnant, high probability seizure free through pregnancy
  - Major organogenesis occurs early in 1st trimester (before she knows)
  - Selection of effective and preferable AEDs prior to pregnancy is critical

Pregnancy - AEDs

- Valproate – XXXXXXXXX
  - Neural tube defects
  - Lower IQ
- Phenytoin – XXXXX
- Phenobarbital – XXXX

Pregnancy – AEDs (cont)

- Carbamazepine – XX
- Topiramate – XXX
  - Low birth weight
- Lamotrigine – X
  - Cleft palate
- Levetiracetam - X

Pregnancy - recommendations

- If no seizures in past year, consider weaning AED
- If unable to wean AED, transition to lower risk AED (LMT, LEV)
- Avoid polytherapy if possible
- Check serum AED level
- Attempt to maintain therapeutic level through pregnancy