Epilepsy in Children

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Epilepsy in Children:
Children Are Different

- Children have different types of seizure disorders
  - Age-related seizures
  - Benign syndromes
- Differential diagnosis is broader
- Etiologies of seizures are different
- Treatments and drugs are different
  - Several AEDs used off-label
  - Different pharmacokinetics
  - Different adverse events
- Children more likely to “outgrow” epilepsy
Evaluation of the Child with Seizure and Epilepsy

- Detailed history
- Clinical examination
- Supportive investigations
  - EEG
  - Ictal video (home video to video EEG)
  - Neuroimaging (MRI, CT scan)
  - Investigation of any suspected underlying condition

Differential Diagnosis of Epilepsy in Children

- Syncope
  - Vasovagal
  - Cardiac
  - Postural
  - Respiratory
    - Breath-holding spells
- Daydreaming
- Migraine
- Transient ischemic events
- Parasomnias
- Normal physiological movements in sleep
  - Benign neonatal sleep myoclonus
Differential Diagnosis of Epilepsy in Children

- Acute rise in intracerebral pressure
- Gastroesophageal reflux
- Vestibular disorders
- Hyperekplexia
- Involuntary movement disorders
  - Paroxysmal kinesogenic choreoathetosis
  - Tics
- Psychotic hallucinations and delusions
- Panic attacks
- Pseudoseizures

Etiology of Epilepsy in Children

- Inherited (genetic)
  - Epilepsy alone
    - “Channelopathies”
Genetic Disorders with Epilepsy

- Idiopathic Epilepsy
- Developmental disorders
  - Brain malformations
  - MR/encephalopathy syndromes (incl autism)
- Neurocutaneous syndromes
- Inborn errors of metabolism/neurodegenerative disease

Common Genetic Disorders with Epilepsy

- Angelman syndrome
- Fragile X Syndrome
- Trisomy 21 (Down Syndrome)
- Rett Syndrome
- Tuberous Sclerosis Complex
- Neurofibromatosis Type 1
- Sturge Weber Syndrome
Etiology of Epilepsy in Children

• Congenital (inherited or acquired)
  • Cortical dysplasia/dysgenesis
  • Cerebral tumor
  • Vascular malformations
  • Prenatal injury

• Acquired
  • Trauma
  • Neurosurgery
  • Infection
  • Vascular disease
  • Hippocampal sclerosis
  • Tumors
  • Neurodegenerative disorders
  • Metabolic disorders
  • Toxic disorders
  • Miscellaneous: celiac, Whipple’s disease, demyelinating disorders, vasculitides
### ILAE Classification of Epilepsies and Epilepsy Syndromes

- **Generalized**
  - Idiopathic generalized epilepsies with age-related onset
  - Cryptogenic or symptomatic generalized epilepsies
  - Symptomatic generalized epilepsies

- **Location-related**
  - Localization-related epilepsies—idiopathic with age-related onset
  - Localization-related epilepsies
  - Central region epilepsies
  - Location-related epilepsies—cryptogenic

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### ILAE Classification of Epilepsies and Epilepsy Syndromes

- Epilepsies and syndromes undetermined as to whether focal or generalized
- Special syndromes
  - Febrile convulsions
**Childhood Epilepsy Syndromes**

- JME (13-19)
- Juvenile absence (10-15)
- GTCS on awakening (6-22)
- Childhood absence (3-7)
- Rolandic epilepsy (4-13)
- Lennox-Gastaut syndrome (1-8)
- Simple febrile seizures (6 mo-5)
- Benign myoclonic epilepsy (1-2)
- Infantile spasms (6 mo-1)
- EMEE/EIEE (0-6 wk)
- Neonatal seizures (0-1 mo)

Adapted from Pellock

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**Infantile Spasms and West Syndrome**

- Onset usually 3-7 months
- Seizure type: flexor or extensor spasm, “salaam”
- EEG pattern: hypsarrhythmia
- Etiologies include
  - Prenatal: cerebral malformations (e.g., TSC), infection, intrauterine hypoxic-ischemic insults (HIE), metabolic disorders
  - Perinatal: HIE, hemorrhage, trauma, infection, metabolic disorder
  - Postnatal: HIE, hemorrhage, trauma, metabolic disorders, infection, neoplasm
Infantile Spasms and West Syndrome: Treatment and Prognosis

- Treatment
  - ACTH
  - Vigabatrin (not released in the United States)
  - Topiramate
  - Ketogenic diet
  - Other (valproate, benzodiazepines, zonisamide)
- Learning disabilities affect 90% of cases and are often severe
- Many evolve into Lennox-Gastaut syndrome
- Mortality 5%

Pediatric Epilepsy Syndromes: Does Etiology Matter?

- Tuberous sclerosis complex (TSC)
  - Relatively common genetic disorder, affecting approximately 1:6000 worldwide
  - 90-95% of individuals will develop epilepsy, particularly during childhood with 70% having onset of seizures first year of life
- Infantile spasms (IS) occur in at least 1/3 of individuals with TSC
  - Some report up to 70% incidence
- TSC is the most common single cause of IS
  - In some series, 25% of symptomatic IS is secondary to TSC
Infantile Spasms in TSC

- Age of onset peaks between 4th and 6th month of life
  - Onset as early as 2nd month of life
- IS preceded by partial seizures in 1/3 of TSC children who develop IS
- Spasms may be asymmetrical, “subtle”
- Baby often develops “indifference,” irritability preceding or coinciding with onset of IS
- Vigabatrin appears particularly effective

TSC: Child with H/O Infantile Spasms (Normal Cognition)

- DOL 6
  - Multiple rhabdomyomas, including mass blocking left ventricular outflow tract
  - Required surgical resection
- 5 months
  - Onset of infantile spasms, with hypersynchronia on EEG
  - Treated with ACTH with initial success, however spasms recurred during taper. Seizures were then difficult to control.
  - Eventually seizure free with carbamazepine
TSC: Child with H/O Infantile Spasms (Normal Cognition)

- Currently in 9th grade
- Seizure free, continues on carbamazepine due to abnormal EEG
- IQ 130 on recent neuropsychological evaluation
Epilepsy Syndromes: Lennox-Gastaut Syndrome

- Intractable seizures of mixed types
  - Atypical absence
  - Myoclonic
  - Tonic
- Mean age of onset: 36 months
- EEG: bilateral slow spike and wave complexes
- 60% with preexisting encephalopathy, 20%-30% with prior infantile spasms
- Learning difficulties in 80%-90% of cases

LGS: Etiologies

- 2/3 to 3/4 with abnormal brain on imaging
- Cortical dysgenesis most common
  - Bilateral perisylvian and central dysplasia
  - Subcortical laminar heterotopias
  - Focal cortical dysplasia
  - Other: hypothalamic hamartoma, Sturge-Weber syndrome, tumors
- LGS uncommon with major brain malformations
  - Lissencephaly, Aicardi syndrome
  - LGS from acquired brain lesions uncommon
LGS: Predictors of Poor Prognosis

- Symptomatic etiology
- Early age of onset
- Prior infantile spasms
- High frequency of tonic seizures
- Frequent episodes of nonconvulsive status epilepticus
- Slow EEG background

Epilepsy, Cognition, and Behavior

- Lennox’s 5 “foes of cognition” in children with epilepsy
  - Heredity
  - Brain damage
  - Seizures themselves
  - Anticonvulsant therapy
  - Psychosocial factors
- Also—interictal EEG abnormalities?
Social Issues in Epilepsy: Impact on Cognition and Behavior

- Factors affecting impact of epilepsy on cognition?
  - Seizure type
  - Location of seizure activity and amount of brain involved
  - Frequency of seizure activity
  - Age of onset
  - Extent of seizure control
  - Side effects of medications

Social Issues in Epilepsy: Impact on Cognition and Behavior

- At least 50% of children with epilepsy have concurrent learning or behavioral problems
  - Compared to 15% of general population
  - Cognitive impairments may affect language, memory, attention, executive function and other abilities critical to normal development
  - Impairments range from mild difficulties to severe dysfunction
Epilepsy in Children
Thiele

Epilepsy, Cognition, and Behavior

- Relationship of epilepsy to autism spectrum disorders
- “Epilepsy syndromes” affecting cognition
  - Continuous spike and wave of slow sleep (CSWS)
  - Landau-Kleffner syndrome
- Interictal EEG abnormalities
  - Treat the EEG?
- Anticonvulsant medications
  - Impact on cognition and behavior
- Psychosocial impact of epilepsy

Relationship of Epilepsy to Autism Spectrum Disorders

- Incidence of autism: 0.7-1.0 per 1000 children
- One third of children with autism have seizure disorder
  - Most common seizure types: complex partial, generalized tonic-clonic, and mixed seizure disorders
  - Autism spectrum disorders may be under diagnosed in children with early onset epilepsy
- 65%-85% of children with autism have developmental delays—many of these children have epilepsy
- Asperger syndrome and pervasive developmental delay (PDD) may be associated with higher incidence of epilepsy

Elective Session
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### TSC: Epileptic Encephalopathy? Case of an 8 yr-old Girl

- 2 mo of age seizure onset
  - Episodes of “eyes going crazy” with horizontal jerking
  - Diagnosis of TSC made: PB started
- 5 mo of age onset of infantile spasms
  - VGB started, IS controlled
  - Change in neurologists; VGB tapered due to concerns of retinal toxicity; IS returned
- Subsequent refractory mixed seizure disorder
  - Txt with TPM, LTG, VPA, LVT

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### TSC: Epileptic Encephalopathy? Case of an 8 yr-old Girl

- TSC manifestations:
  - Skin: angiofibroma, forehead plaque, shagreen patch, hypopigmented macules
  - Cardiac rhabdomyoma
  - Renal angiomyolipoma bilaterally
  - TSC2 mutation
- Neuro exam
  - Very poor eye contact
  - Paucity of movements although will reach for objects R>>L
TSC: Epileptic Encephalopathy?
Case of an 8 yr-old Girl

- 10 seizures per day
- Mixed seizure types
  - “Staring seizures”
  - Drop seizures
  - “Thrashing seizures”
  - “Laughing seizures”
- Global developmental impairment
  - Nonverbal
  - Nonambulatory (had been walking, stopped 1 yr prior)
- Very poor eye contact

8 year old Girl with TSC:
Background Sleep EEG
8 year old Girl with TSC: Tuber Burden, and Cystic Changes on MRI
TSC: Epileptic Encephalopathy?
Case of an 8 yr-old Girl

• Post operative hospitalization:
  • Markedly improved eye contact
  • Increased use of L UE
• 12 month post op:
  • Seizures reduced over 75%
  • Significant developmental gains
    • Improved social interactions
    • Improved comprehension
    • Improved motor function, pulling to stand, taking steps
    • Significant changes in IEP

TSC and Autism: ? Epileptic Encephalopathy

• Refractory epilepsy and autism are both very common in TSC
• What is the relationship?
  • Many variables, how can they be sorted out?
  • What impact does relationship have on clinical care,
    • e.g. Resective surgery for epileptic encephalopathy?
• And, what causes epilepsy and autism in TSC?
• And, is epileptic encephalopathy an important consideration in many kids with autism?
Syndrome of CSWS

- Or: electrical status epilepticus of sleep (ESES)
- Definition: prolonged generalized spike and wave discharges on EEG, occupying at least 85% of slow sleep tracing
- Can occur in children with normal development

Patry, et al. 1971

Syndrome of CSWS

- Clinical features
  - Drop in IQ
  - Aphasic difficulties
  - Memory loss
  - Impairment of temporospatial orientation
  - Apraxia and psychiatric disturbances
Syndrome of CSWS

• Treatment
  • High-dose diazepam protocol
    • Initial 1 mg/kg dose, with continuous video EEG monitoring
    • “Maintenance” dose of 0.5 mg/kg qhs
    • Follow-up EEG
  • Corticosteroids
    • Prednisone (6-month course)
  • Anticonvulsant medications
    • Benzodiazepines

Landau-Kleffner Syndrome: Acquired Aphasia-Epilepsy Syndrome

• Clinical features
  • Normal initial psychomotor development
  • Acquired childhood aphasia
  • Epilepsy in 70%, seizures may be rare, and often disappear by 15 years of age
  • Paroxysmal EEG abnormalities (mainly bitemporal)
  • No demonstrable focal brain lesion
  • Stabilization of disease after variable time (improvement)
## Landau-Kleffner Syndrome: Acquired Aphasia-Epilepsy Syndrome

- Acquired aphasia
  - Onset variable, most often subacute, progressive with fluctuation
  - Verbal auditory agnosia (but all types of aphasia can occur)
- Male predominance (2:1)
- Usually no family history
- Psychomotor disturbances in 72% (hyperkinesis)
- Seizure and epilepsy in 72%
  - Semiology poorly studied

## Landau-Kleffner Syndrome: Evaluation and Treatment

- Evaluation
  - (at Children’s Hospital, Boston, Mass)
    - Continuous EEG monitoring
    - FM auditory evoked response (FMAER)
- Treatment
  - Corticosteroids
  - High-dose diazepam
  - AEDs: valproate
  - Surgery?
Landau-Kleffner Syndrome: Prognosis

- Prognosis
  - Epilepsy typically responds to medication and resolves
  - Aphasia persists after EEG normalization
  - 50% able to lead normal life
  - Prognosis is better if
    - Onset is after 6 years of age
    - Speech therapy is instituted early

Landau-Kleffner Syndrome and CSWS: Common Features

- Onset during childhood
- Deterioration of cognitive functions that were previously acquired normally
- Absence of structural lesion
- Type of seizure
- EEG pattern during sleep and wakefulness
- Pharmacologic reactivity
Interictal EEG Abnormalities: Should We Treat the EEG?

- Do interictal epileptiform discharges affect cognition and behavior?
  - Case: 12-year-old boy with h/o head injury at 7 months, subsequently on low-dose AED due to abnormal EEG
  - Learning difficulties in school, neuropsychological profile “matched” EEG
  - After change in AED and optimization of dose, marked improvement in EEG and neuropsychological testing
- Are seizures really the “tip of the iceberg”?

Anticonvulsant Medications: Cognitive and Behavioral Effects

- AEDs have both behavioral and cognitive effects on children
  - Phenobarbital, benzodiazepines: irritability, poor impulse control, depression
  - Phenobarbital and phenytoin slow and impair cognitive functioning of children
  - Topiramate can have significant cognitive adverse effects
- Other new and old AEDs?
- Worse with polytherapy, high therapeutic blood levels
- How to monitor?
Effect of Seizure-Related Factors on Child’s Behavior

- Seizure type
- Seizure control
  - Poor seizure control correlates with increased likelihood of behavioral difficulties, also with lower cognitive functioning
- Effects of antiepileptic medications
  - Polytherapy and high therapeutic levels increase risk of difficulties

Epilepsy in Childhood: Psychosocial Issues

- Epilepsy is a chronic illness
  - Impact on child and family
  - Unpredictability—child never knows when seizure is going to happen
    - Leads to feeling of lack of control, fearfulness, anxiety, need to be dependent
  - Low self-esteem, which can ultimately lead to depression
  - Lack of control over body during seizure episode
  - Reaction of peers to seizure—may be negative and rejecting
Epilepsy in Childhood: Psychosocial Issues

- Epilepsy and the schools
  - Seizure activity at school increases child's sense of lack of control
  - Stigma from peers and teachers
  - Lack of awareness by educators can lead to underestimation of child's academic abilities as well as unnecessary absences
- Epilepsy and adolescence
  - Epilepsy impacts maturation due to increased dependence
  - Increased anger and noncompliance with medications
- Interface with medical system

Social Issues in Epilepsy: Treating the Child, Not Just the Seizures

- The whole-child approach
  - Controlling seizures important, but only part of the equation
  - Important to enable a child with epilepsy to reach their full potential in terms of learning, socializing, communicating and enjoying life
    - Educating child and family about epilepsy
    - Educating child’s educators about his/her epilepsy and effects on learning
    - Ensuring child has an accepting and understanding peer group

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Social Issues in Epilepsy:
Treating the Child, Not Just the Seizures

Children with epilepsy who are seizure free are still handicapped if they and those around them don’t understand their disease!

Social Issues in Epilepsy

- What we (MGHfC) are trying to do:
  - Parent Networks
  - Sibling Workshops
  - Educational website: growing up with epilepsy
  - Educator conferences
  - Epilepsy and Karate program
  - Epilepsy and Yoga program
  - Ketogenic Diet Halloween party
  - Rock climbing
Social Issues in Epilepsy: Safety Precautions

“What protecting a child with epilepsy from harm is important, but so too is providing opportunities for the child to fully experience life.”

www.massgeneral.org/childhoodepilepsy