Pediatric Neuroimaging in Epilepsy

Bhagwan Moorjani, MD, FAAP, FAAN
Hope Neurologic Center
La Quinta, CA
Neuroimaging in Childhood

• Neuroimaging issues are distinct from adults
• Sedation/anesthesia
• Motion artifacts
• Requires knowledge of normal CNS developmental (i.e. myelin maturation)
• Contrast media
• Parental anxiety
Diagnostic Approach

• Age of onset
• Static versus Progressive
  – Look for treatable causes
  – Do not overlook abuse, Manchausen if all is negative
• Phenotype presence (syndromic, Head Circumference, Neurocutaneous Syndrome, systemic involvement)
• Predominant symptom (Epilepsy, developmental delay, weakness/motor, psychomotor regression, cognitive/dementia)
Neuroimaging in Epilepsy

• Peak incidence in childhood
• Occurs as a co-morbid condition in many pediatric disorders (birth injury, dysmorphism, chromosomal anomalies, developmental delays/regression)
• Many neurologic disorders in children have the same chief complaint
Epilepsy: Etiology vs Age of Onset

- Perinatal injury
- Metabolic defect
- Congenital malformation
- Infection
- Genetic epilepsy
- Postnatal trauma
- Brain tumor
- Vascular disease

Age (yr)
Congenital Malformation

- Characterized by their anatomic features
- Broad categories: based on embryogenesis
  - Stage 1: Dorsal Induction: Formation and closure of the neural tube. (Weeks 3-4)
  - Stage 2: Ventral Induction: Formation of the brain segments and face. (Weeks 5-10)
  - Stage 3: Migration and Histogenesis: (Months 2-5)
  - Stage 4: Myelination: (5-15 months; matures by 3 years)
Etiology of Epilepsy:
Developmental and Genetic Classification of Cortical Dysplasia

1. Secondary to abnormal neuronal and glial proliferation/apoptosis
2. Secondary to abnormal neuronal migration
3. Secondary to abnormal cortical organization or late migration
4. Not otherwise classified
   • IEM
   • Other unclassified dysplasia
Gray Matter Heterotropia

- displaced masses of nerve cells (gray matter)
- most common: small nest adjacent to lateral ventricles
- Range from nodular to band heterotropia to schizencephaly, lissencephaly and polymicrogyria
- clinical: seizures
- MRI: isointense with gray matter in all sequence

- Subependymal heterotropia (most common)
- Band heterotropia (double cortex)
- Lissencephaly
- Cobblestone cortex (lis 2)
- Subcortical heterotropia
Subependymal heterotropia

T1W – multifocal GM nodules lining lateral ventricle, also in the frontal WM
Subcortical heterotropia

T2W – blurred curvilinear line extending from cortex to ventricular surface
Polymicrogyria

- multiple abnormal tiny indentation along brain surface (5-7mm)
- abnormal cortical histology
- can be unilateral
- MRI: decreased number of broad, thick, smooth gyri

T2W – blurring of gray white junction (open arrow)
Nodular appearance
polymicrogyria

T2W - Bilateral perisylvian/suprasylvian polymicrogyria
Polymicrogyria

T1W – irregular interface with adjacent white matter
Double cortex

T2W – decreased sulcation
primitive sylvian fissure (open arrow),
Thick band of incompletely migrated cortex (arrow)

Cortex inversely proportional to band heterotropia
Double cortex

T1W - asymmetry of paramedial parietal region
Heterotopic Gray matter
Double cortex

T1W - GM heterotropia right parieto-occipital region (open arrow)
Thinning of overlying cortex (arrow)
Double cortex

6 month old with seizures

T2W – thin band of GM in the deep white matter
Pachygyria

- thick and more completely developed gyri
- commonly diffused with relative sparing of temporal lobes
- associated with: agenesis of CC and heterotopias
- clinical: microcephaly, seizures, MR, developmental delay
- MRI: circumferential band of high signal on T2 within the cortex
Lissencephaly

- Severe form of neuronal migration Disorder
- Can be seen in:
  - Isolation
  - Miller Dieker Syndrome
  - TORCH infection (CMV)
- Clinical S/S:
  - Mental Retardation
  - Intractable Epilepsy
  - Microcephaly
Lissencephaly Imaging

• Hourglass or figure of 8
  – Shallow sylvian fissure
• LIS 1: parietal-occipital
• X-LIS: Subfrontal/temporal
• 3 layers may be seen in neonates on T2W
  – Outer layer – thin, smooth
  – Intervening cell sparse layer
  – Deeper thick layer – mimicking band heterotropia
• Posterior > Anterior involvement in LIS 1
lissencephaly

T2W – complete absence of cerebral sulcation

Cerebellum is normal

Hyperintense cell sparse zone separates the thin cortical ribbon from the thicker band of disorganized neurons
Miller Dieker

T1W

Typical midline calcification

Thin outer GM layer

Cell sparse WM layer

Thick inner GM band
Lis 1

T2W
Severe parietal-occipital involvement (Classic pattern)
Cell sparse WM layer posteriorly
Agyria

- Complete lissencephaly
- Smooth brain

Identified by figure eight due to shallow sylvian fissures.
Schizencephaly

- Gray matter-lined cleft that extends from the ventricular ependyma to the pia.
- Unilateral or bilateral
- Two types:
  - Closed lip (type I)
  - Open lip (type II)
Schizencephaly Imaging

• Transmantle gray matter lining clefts
  – Dimple in wall of ventricle if closed or narrow
• Frontal and Parietal lobes near central sulcus
• Distinction of GM lining cleft can be difficult prior to myelination
• DVA overlie cleft seen on MRV
Schizencephaly
Differential Diagnosis

• Porencephaly
  – Lined by gliotic white matter
  – No dysplastic gray matter

• Semilobar Holoprocencephaly
  – Can mimic bilateral open lip schizencephaly
Schizencephaly
Schizencephaly
Schizencephaly
Hemimegalencephaly

- Primary hamartomatous malformation
- Onset usually in neonatal period
- Catastrophic
- One type of onset is Tonic Seizure (Ohtahara Syndrome)
- Can be asymmetric and often precede or overlap with West Syndrome (IS)
- IS = 50%
Hemimegalencephaly

• No differences between Isolated or Syndromic type.
• Plain Skull Films: look for macrocrania & asymmetry.
• May see intracranial calcifications & bony dysplasia
• US: prenatal may suggest HME, may see macrocephaly, ventricular asymmetry with enlargement of lateral ventricle
  – Prenatal: may see unilateral ventricular dilation with hemispheric enlargement
Hemimegalencephaly Imaging

- **CT & MRI:**
  - Gross asymmetry
  - 1 hemisphere enlarged
    - Posterior falx and occipital pole displaced to contralateral side
  - Dysplastic Cortex
  - Asymmetry of Ventricular System

- 4 points of abnormal ventricle.
  - 1. Straightened frontal horns (pointed)
  - 2. mild-extreme dilation of lateral ventricle
  - 3. reverse of contralateral horn (mass effect appearance)
  - 4. colpocephaly (disproportionate developmental dilation of occipital horn of lateral ventricle) in all grades of HME
Hemimegalencephaly

FLAIR – bright signal in WM of abnormal hemisphere
The only disorder that enlarges both hemisphere and ipsilateral ventricle
FCD with Balloon Cells

- Abnormal gyral pattern when large
- Blurring of gray-white junction
- Abnormal tissue: cortex to border of lateral ventricle
- Typically associated with TS
- Solitary – no other TS features
- T2 hyperintense “comet tail” from cortex to ventricle
  - Best seen on flair
FCD - Balloon Cell

PD FSE – focal thickening with increased signal of expanded gyrus
FCD with balloon cell

T2W – juxtacortical signal change
Thin line of signal change tracking along the expected Course of the radial glial fibers to the Subependymal margins
FCD with balloon cell

FLAIR – gyral expansion and thin signal change extending to the ventricle
DNET

- Intractable epilepsy
- Focal deficits
- More common 2\textsuperscript{nd} and 3\textsuperscript{rd} decade
- Considered part of abnormal neuronal/glial proliferation - neoplastic
- MRI Findings:
  - T1 hypointense
  - T2 hyperintense
  - Modest to no enhancement
  - Scalloping
  - Lack of mass effect, edema
DNET

T2W – 5 year old with seizures

Multicentric bubbly DNET with involvement of body of the caudate nucleus
DNET

FLAIR – characteristic appearance

Cortically based, sharply demarcated wedge shaped mass with hyperintense rim

Points towards the ventricle

No edema
DNET

T1W-C+

Cystic component with multiloculated appearance

No solid enhancement
Metabolic Epilepsies
MRI Features of Metabolic Diseases

• Common Abnormalities
  – Atrophy
  – Symmetry

• Infrequent
  – Enhancement

• Myelination abnormalities
• Malformation
Neurometabolic-Degenerative Disorders

• Knowledge of normal myelination pattern is essential

• General rules:
  – Caudal to cranial
  – Posterior to anterior

• MRI provides the best imaging modality
  – T1 matures at 12-14 months
  – T2 matures at 24-26 months
Neurometabolic-Degenerative Disorders

- **Type of myelination involvement**
  - Delayed myelination
  - Demyelination
  - Dysmyelination

- **Nervous system involvement**
  - Brainstem involvement
  - Cerebellar involvement
  - Spinal Cord involvement

- **Tissue Involvement**
  - Gray matter involvement
  - White matter involvement
1 month

9 months

36 months

From Alberico
Factors to Consider

- Age of Onset
- Degree of derangement
- Abnormal metabolite
  - Deficiency or excess
- Stage of the disease process
- Phenotype
Leukodystrophies

- Abnormal signal in white matter
- Symmetric usually
- Periventricular, deep or subcortical in location
- Failure to achieve myelination milestones
- MRS abnormalities reflect neuronal loss and increased cellular turnover
- Some have contrast enhancement
  - ALD: zone of active inflammation
  - Alexander: ventricular lining, periventricular rim, frontal WM, optic chiasm, fornix, BG, thalamus, dentate nucleus
Leukodystrophies
Differential Diagnosis

- Radiation and Chemotherapy injury
- Viral encephalitis
- ADEM
- MS
- In neonates: HIE
  - Periventricular pattern
Head Circumference

Macrocephalic
- Canavan
- Alexander
- Tay Sachs (GM2 gangliosidosis)
- L-2-hydroxyglutaric aciduria

Microcephalic/Normal
- MLD
- Pelizaeus Merzbacher disease
- Zellweger Disease
- Krabbe
Alexander Disease

• Clinical S/S: macrocephaly, seizures
• Mutation: GFAP, Chromosome 17q21
• Imaging
  – Extensive WM changes with frontal predominance
  – Abnormal signal in BG and thalami
  – Enhancement: ventricular lining, periventricular rim, frontal WM, optic chiasm, fornix, BG, thalamus, dentate nucleus

• Give contrast to all unknown cases of hydrocephalus and abnormal WM
Alexander Disease

T1W-C+:
Enhancement of the periventricular rim, caudate heads and putamen bilaterally

Rabbit ear – characteristic of Alexander
Nodular appearance of frontal PV rim
Alexander Disease

FLAIR – less severe disease
High signal in the anterior and posterior rims and WM with frontal predominance
Alexander Disease

T1W-C+ - enhancement of bifrontal PV WM, PV rim and caudate head. Less intense patchy enhancement in putamen and thalamus
Alexander Disease

T2W – advanced disease
Symmetric, hyperintense cerebral WM and deep gray structures
Swollen caudate head and fornices
Hyperintensity in external and extreme capsule – claustra stands out
Alexander Disease

FLAIR – large foci of cystic destruction in frontal WM and caudate head
These are late findings
Canavan Disease

• Clinical S/S: Macrocephaly, hypotonia
• Imaging:
  – Diffuse T2 hyperintensity preferentially involves subcortical U fibers
  – Spares internal capsule and corpus callosum
  – Involves thalamus, globus pallidus ± dentate
  – Spares caudate and putamen
  – MRS shows marked elevation of NAA peak
Canavan Disease

T2W – diffuse cerebral WM hyperintensity. Involvement of subcortical U fibers
Canavan Disease

T2W – 6 month old
Diffuse increase signal cerebral WM including thalamus and right globus pallidus
Sparing of internal capsule, CC and putamen
Canavan Disease

T2W: infant
Marked hyperintense signal and swelling throughout WM
Striatum as island of tissue
Canavan Disease
Differential Diagnosis

• Maple Syrup Urine Disease
  – Elevated branch chain AA

• Pelizaeus-Merzbacher Disease
  – Spares GP and thalami

• Alexander Disease
  – Enhances
  – Predominantly frontal WM
Hypomyelination Disorder

- Areas to assess: internal capsule, pyramidal tracts, peripheral frontal lobe WM
- T1 signal reflects presence of myelin
  - Children < 10 months
    - Myelinated WM - hyperintense
  - Children > 10 months
    - Mature WM - hypointense
- T2 reflects displacement of water
  - Children > 10 months
    - Mature WM - hypointense
Pelizaeus-Merzbacher Disease

- Clinical S/S: microcephaly, hypertonia, stridor
- Deficiency of proteolipid protein (PLP)
- Hypomyelination disorder
- Imaging
  - Variable
  - Nonspecific and symmetrical abnormality of WM
  - Lack of myelin
Pelizaeus-Merzbacher Disease

T2W: 13 year old absence of normal hypointense WM signal

This is normal for a 6-8 month old child
Hypomyelination

T2W – 2 year old

• Diffuse lack of T2 hypointense myelin in deep WM, corpus callosum and internal capsule

At this age nearly all WM structures should be myelinated (hypointense on T2W.)
Metachromatic Leukodystrophy

- Decreased arylsulfatase A
  - Central and peripheral demyelination
- Imaging
  - Confluent butterfly-shaped increased T2 signal deep cerebral WM
    - Spares U fibers in early disease
    - Involves U fibers in late disease
  - Sparing of perivenular myelin producing the tigroid appearance
  - No enhancement of WM
  - May have enhancement of cranial nerves and cauda equina
MLD

FLAIR – bilateral, symmetric periventricular and deep WM changes sparing U-fibers
MLD

T2W – tigroid appearance of WM
Due to preservation of myelin in perivascular regions
Krabbe Disease

• aka Globoid cell leukodystrophy
• Clinical S/S: irritability
• Juvenile form: protracted course with slow rate of progression
• CT: hyperdensity in thalamus, BG
• MRI Imaging:
  – Faint hyperintensities in thalamus and BG (T1W)
  – Ring like appearance around dentate nucleus (T2W)
  – PV WM hyperintensities (T2W)
    • Initially spares U fibers
  – Enlarged optic nerves and cranial nerves (T1W)
• MRS: increased choline, myoinositol, decreased NAA, lactate accumulation
Krabbe Disease
CT Scan

Faint hyperdensity in the lateral thalami, from presumed Ca++ deposits
CT more sensitive than MR in early course
Krabbe Disease

FLAIR – focal symmetric hyperintensity capsular portion of corticospinal tracts.
Krabbe Disease

FLAIR – juvenile onset – symmetric hyperintensity in parietal WM sparing subcortical U fibers
Krabbe Disease

T2W – advanced disease – atrophy, hypointensity in BG and Thalami
SSPE

• Nonspecific leukoencephalopathy
• MRS:
  – decreased NAA/Cr
  – Increased Cho/Cr; Ins/Cr and Lac-Lip
SSPE

Proton Density:
Inhomogeneous hyperintensity bilaterally, asymmetric involving WM and cortex

Biopsy - SSPE
Gray Matter Metabolic Disorder

- Leigh Disease
- 3-methylglutaconic aciduria
- Biotin dependent encephalopathy
- Methylmalonic acidemia
Leigh Syndrome

- Progressive neurodegeneration
- Respiratory chain disorder
- Clinical S/S: psychomotor delay/regression
- Imaging:
  - Bilateral symmetric increased T2/FLAIR signal
    - Putamen>caudate>GP, periaqueductal gray, SN/STN, dorsal pons, cerebellar nuclei
  - Restrictive diffusion in areas of acute disease
- MRS: increased lactate; decrease NAA, increase choline
Leigh Syndrome

- DWI – reduced diffusion in thalamus
- T2W – subtle thalamic involvement
  - Thalamic involvement may be isolated when patient becomes symptomatic
  - DWI shows abnormality better than T2W
Leigh Syndrome

T2W – hyperintensity in caudate head, putamen, periaqueductal GM

Common site of involvement due to ETC complexes I and II