Potpourri of Pediatric Neurology

February 25, 2017

Neil Friedman MBChB
Director for Pediatric Neurosciences
Case 1: A Case Of The Jitters
Diagnosis?
Differential Diagnosis: Neonatal/Infantile myoclonus

- Myoclonic epilepsy
  - Benign
  - Progressive myoclonic epilepsies (PME)
- Benign neonatal/infantile sleep myoclonus
- Hyperekplexia
- Myoclonic tics
- Opsoclonus-myoclonus syndrome
- Spinal myoclonus
- Other
Diagnosis: Midazolam-induced Myoclonus

- Intravenous bolus administration of midazolam (Versed) is an uncommon but well described cause of myoclonic movements in very low birth weight premature Infant.
Diagnosis: Sleep myoclonus

- Myoclonus is part of normal sleep physiology, as paradoxical excitation in rapid-eye-movement sleep.
- Beginning in fetal life, this is most abundant during the first 6 to 8 months postnatally and persists through life as fragmentary nocturnal myoclonus.
- Hypnic jerks, or myoclonus on sleep initiation, are associated with the sensation of falling.
Myoclonus

- Brief involuntary muscle jerk originating in the central nervous system\textsuperscript{1}
  - Cortical – tends to be focal and distal and typically found in the arm.
  - Subcortical – tends to be both proximal and distal generalized myoclonus, involving both agonist and antagonist muscle groups
  - Spinal – tends to be limited to muscles innervated by a few or multiple spinal segments and affects predominantly flexor muscles

\textsuperscript{1}Pranzatelli M. Seminars in Pediatric Neurology, 2003;10:41-51
Myoclonus Continued

- It is a paroxysmal event that may appear as an isolated finding or as a symptom of many diseases
- Physiologic myoclonus occurs episodically throughout life as hiccoughs and hypnic (sleep) jerks
Clinically Different Forms of Myoclonus

- Three types:
  - Spontaneous
  - Reflex
  - Movement-induced/action myoclonus (most common)

- Myoclonus is also distinguished from other movement disorders by its unusual association with epilepsy and ataxia
Case 2: A Frightful Awakening
History

• 10 year-old girl with long standing history of sleep disturbances – brief, usually < 1 minute
• Abrupt arousal from sleep, vocalization (grunt, moan, or a single word)
• Complex and sometimes violent automatisms – sits up or jumps up, frightened expressions, bipedal and bimanual automatisms
History Continued

- Other times prominent tonic and dystonic features, often associated with preservation of consciousness
- Having problems with daytime somnolence
- Family history of sleep walking and night terrors
Diagnosis?
Differential Diagnosis

- Parasomnias – night terrors, nightmares
- Movement disorder - nocturnal paroxysmal dystonia, restless leg syndrome
- Epilepsy
- Psychogenic non-epileptic events
Investigations
Diagnosis:
Autosomal Dominant Nocturnal Frontal Lobe Epilepsy
ADNFLE

- Three gene loci identified to date
- May be sporadic
- Occurs almost exclusively from sleep although up to one third of patients may have infrequent daytime seizures
- Frequent, nearly every night, often clusters of brief (20–50 seconds) seizures
- Spectrum of clinical manifestations, ranging from brief, stereotyped, sudden arousals to more complex dystonic-dyskinetic-hyperkinetic seizures or tonic manifestations
## Hypermotor Seizures – Clinical Pattern

<table>
<thead>
<tr>
<th>Seizure type</th>
<th>Agitation</th>
<th>Motor Signs</th>
<th>Non Motor Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hypermotor behaviors</td>
<td>Facial affects</td>
</tr>
<tr>
<td>Type 1</td>
<td>Marked</td>
<td>Kicking, boxing</td>
<td>Fear</td>
</tr>
<tr>
<td></td>
<td>Semi-purposeful</td>
<td>Body rocking</td>
<td>Anger</td>
</tr>
<tr>
<td>Type 2</td>
<td>Mild</td>
<td>Horizontal movements or rotation of trunk and pelvis</td>
<td>Tonic – dystonic posture</td>
</tr>
</tbody>
</table>
# Parasomnias versus Night-time Seizures

<table>
<thead>
<tr>
<th></th>
<th>Parasomnias</th>
<th>Nocturnal Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing</strong></td>
<td>Linked to sleep stage</td>
<td>Less often</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Usually &gt; 5 minutes</td>
<td>Brief, &lt;1-2 minutes</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Variable</td>
<td>Stereotyped; Abrupt onset out of sleep</td>
</tr>
<tr>
<td><strong>Precipitating factors</strong></td>
<td>Fatigue, stress, fever</td>
<td>Lack of sleep</td>
</tr>
<tr>
<td><strong>Daytime sleepiness</strong></td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Therapy</strong></td>
<td>Imipramine; Clonazepam</td>
<td>Seizure medication</td>
</tr>
</tbody>
</table>

---

Cleveland Clinic Children's  

IPS 2017
Pearls

• May be associated with auras – may be woken by a relatively non-specific aura, such as a sensation of “their breath being stuck in their throat,” a shiver, or a feeling in the limbs
  - Aura appears to be more common in ADNFLE than sporadic NFLE
• Awareness may be preserved in at least a proportion of seizures, with individuals experiencing fear or panic

• A significant number of individuals with NFLE also report a personal or family history of events such as benign parasomnias, sleepwalking, and sleep terrors
Case 3: Things That Go Bump In The Night
History

- 4 year old boy with abrupt onset rhythmic movement during sleep
- Occurs in clusters – lasting up to 5 minutes
- Normal development
- No past medical history of note
- Normal neurological examination
Diagnosis?
Jactatio capitis nocturna (head banging)

• Head banging is a subtype of sleep related rhythmic movement disorder (RMD)
• It mainly affects infants and children
• Involves large muscle groups (especially neck and trunk muscles) that engage in repetitive, stereotyped, and rhythmic movements
• Movements emerge predominantly during drowsiness or sleep
• Frequency of 0.5-2 seconds, and with clustered episodes usually lasting less than 15 minutes
ICSD Diagnostic criteria for RMD

- Rhythmic body movements during drowsiness or sleep (0.5-2Hz).
- At least one of the following types is present:
  - Head-banging
  - Head rolling type
  - Body rocking
  - Body rolling
Typical Movements

• Head banging typically occurs with the child lying face down – banging the head down into a pillow or mattress
• In the upright position, the head is banged against the wall or headboard repeatedly or the upper body may be rocked
• Body rocking is typically done with the entire body while on the hands and knees
Rhythmic movement Disorder

- Usually disappears by age 5
- Continues in 6% of 5 year-olds and in 3% of 13 year-olds
- Benign in the large majority of cases
- Most children and adults who have rhythmic movement disorder are healthy, although the condition is more common in children with autism and other developmental disabilities
TREATMENT

• Typically none
• Medications (rarely)
  - Benzodiazepine (Clonazepam)
  - Antidepressant citalopram
  - Hydroxyzine
  - Antihistaminines
  - Gabapentin
Case 4: CP Or Not CP – is that the right question?
History

- 6 year-old boy presented at 14 months of age with lower extremity hypertonia
- Born at term
- Family noticed intermittent episodes of leg “twitching”/shaking several times a day, usually at rest, and stopped with repositioning of the legs
- Delayed motor development due to scissoring of legs interfering with walking
Examination

- Bilateral spasticity of lower extremities with hyperreflexia, sustained clonus of ankles and legs, and cross adductor response
- Gait: see video
- Remainder of examination normal
Diagnosis?
Differential Diagnosis

- Spastic diplegic cerebral palsy
- Structural
  - Chiari malformation; atlanto-axial subluxation
- Leukodystrophy:
  - Krabbe’s, MLD, etc.
- Metabolic:
  - Arginase deficiency, abetalipoproteinemia
- Genetic:
  - Dopa-responsive dystonia; Pelizaeus-Merzbacher disease (mild form); hereditary spastic paraplegia (autosomal recessive; X-linked)
- Infection: myelitis
Family History

• Significant for lower extremity paraplegia in multiple maternal family members – varying severity, but all with onset in first few years of life

• Mother, 2 maternal uncles, maternal grandfather, maternal great grandmother similarly affected
Special Studies

- Brain MRI normal
- Spine MRI normal
Diagnosis?

- Progressive spasticity of legs with clonus
- Early onset
- + Family history
- Normal brain and spine MRI scan
Hereditary Spastic Paraplegia

- DNA testing for hereditary spastic paraplegia – **positive** for pathogenic mutation in SPG3A gene consistent with autosomal dominant HSP
Hereditary Spastic Paraplegia: Overview

• Group of genetic disorders characterized by slowly progressive lower-extremity weakness and spasticity

• Age of onset, rate of progression, associated symptoms, degree of muscle weakness and spasticity, overall severity vary greatly from one person to another, or among individuals within the same family
Classification

• Uncomplicated
• Complicated/complex
Uncomplicated HSP

• Neurologic impairment is limited to progressive lower-extremity spastic weakness
• Mild diminution of lower-extremity vibration sensation
• Hypertonic urinary bladder disturbance
Complicated or “Complex” HSP

- Other neurologic findings such as seizures, dementia, extrapyramidal disturbance, or peripheral neuropathy
- Other system involvement
  - Skin disease (ichthyosis)
  - Hearing (SNHL) and vision abnormalities (optic atrophy, cataracts, retinal degeneration)
  - Scoliosis
<table>
<thead>
<tr>
<th>Gene symbol</th>
<th>Protein name</th>
<th>Main phenotype</th>
<th>Cell biological function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Membrane traffic-related</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG3A</td>
<td>Atlastin-1</td>
<td>AD Pure</td>
<td>ER morphogenesis, BMP signalling</td>
</tr>
<tr>
<td>SPG4 (also known as SPAST)</td>
<td>Spastin</td>
<td>AD Pure</td>
<td>ER morphogenesis, Endosomal traffic, BMP signalling, Cytoskeleton regulation</td>
</tr>
<tr>
<td>SPG6 (also known as NIPA1)</td>
<td>NIPA1</td>
<td>AD Pure</td>
<td>Cytoskeletal regulation</td>
</tr>
<tr>
<td>SPG8 (also known as KIAA0196)</td>
<td>Strumpellin</td>
<td>AD Pure</td>
<td>Endosomal trafic, BMP signalling</td>
</tr>
<tr>
<td>SPG10 (also known as KIF5A)</td>
<td>KIF5A</td>
<td>AD Complex</td>
<td>Endosomal morphogenesis, Cytoskeleton regulation</td>
</tr>
<tr>
<td>SPG11 (REF. 103)</td>
<td>Spatasiin</td>
<td>AR Complex</td>
<td>Membrane traffic?</td>
</tr>
<tr>
<td>SPG15 (also known as ZFYVE26)</td>
<td>Spastizin (also known as ZFYVE26 or FYVE-CENT)</td>
<td>AR Complex</td>
<td>Membrane traffic?</td>
</tr>
<tr>
<td>SPG17 (also known as BSCL2)</td>
<td>Seipin</td>
<td>AD Complex</td>
<td>ER membrane protein, Lipid droplet biogenesis</td>
</tr>
<tr>
<td>SPG20 (REF. 107)</td>
<td>Spartan</td>
<td>AR Complex</td>
<td>Endosomal traffic, BMP signalling, Lipid droplet biogenesis, Mitochondrial?</td>
</tr>
<tr>
<td>SPG21 (REF. 108)</td>
<td>Maspardin</td>
<td>AR Complex</td>
<td>Endosomal traffic</td>
</tr>
<tr>
<td>SPG31 (also known as REEP1)</td>
<td>REEP1</td>
<td>AR Complex</td>
<td>Endosomal traffic</td>
</tr>
<tr>
<td><strong>Mitochondrial</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG13 (also known as HSPD1)</td>
<td>HSP60</td>
<td>AD Pure</td>
<td>Mitochondrial chaperone</td>
</tr>
<tr>
<td>SPG7 (REF. 111)</td>
<td>Paraplegin</td>
<td>AR Complex</td>
<td>Mitochondrial protease</td>
</tr>
<tr>
<td><strong>Myelination</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG2 (also known as PLP1)</td>
<td>PLP</td>
<td>XLR Complex</td>
<td>Myelin protein</td>
</tr>
<tr>
<td>SPG35 (also known as FA2H)</td>
<td>Fatty acid 2-hydroxylase</td>
<td>AR Complex</td>
<td>Hydroxylation of myelin lipids</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG1 (also known as L1CAM)</td>
<td>L1CAM</td>
<td>XLR Complex</td>
<td>Cell adhesion and signalling</td>
</tr>
<tr>
<td>SPG5 (also known as CYP7B1)</td>
<td>CYP7B1</td>
<td>AR Pure</td>
<td>Cholesterol metabolism</td>
</tr>
<tr>
<td>SPG30 (REF. 117)</td>
<td>Neuropathy target esterase</td>
<td>AR Complex</td>
<td>Phospholipid homeostasis, Target of organophosphates</td>
</tr>
<tr>
<td>SPG42 (also known as SLC33A1)</td>
<td>SLC33A1</td>
<td>AD Pure</td>
<td>Acetyl-CoA transporter</td>
</tr>
<tr>
<td>SPG48 (also known as KIAA0415)</td>
<td>KIAA0415</td>
<td>AR Complex</td>
<td>DNA repair</td>
</tr>
</tbody>
</table>

AD, autosomal dominant; AR, autosomal recessive; BMP, bone morphogenetic protein; CYP7B1, 25-hydroxycholesterol 7-alpha-hydroxylase; ER, endoplasmic reticulum; FA2H, fatty acid 2-hydroxylase; HSP60, heat shock protein 60; KIF5A, kinesin heavy chain isoform 5A; L1CAM, neural cell adhesion molecule L1; NIPA1, non imprinted in Prader-Willi/Angelman syndrome 1; PLP, myelin proteolipid protein; REEP1, receptor expression-enhancing protein 1; SPO, spastic paraplegia; SLC33A1, solute carrier family 33 (organic anion transporter) member 1; XI, X-linked recessive.
<table>
<thead>
<tr>
<th>Gene symbol</th>
<th>Protein name</th>
<th>Main phenotype</th>
<th>Cell biological function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Membrane traffic-related</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG3A</td>
<td>Atlastin-1</td>
<td>AD Pure</td>
<td>ER morphogenesis, BMP signalling</td>
</tr>
<tr>
<td>SPG4 (also known as SPAST)</td>
<td>Spastin</td>
<td>AD Pure</td>
<td>ER morphogenesis, Endosomal traffic, BMP signalling, Cytoskeletal regulation</td>
</tr>
<tr>
<td>SPG17 (also known as BSCL2)</td>
<td>Seipin</td>
<td>AD Complex</td>
<td>ER membrane protein, Lipid droplet biogenesis</td>
</tr>
<tr>
<td>SPG20 (REF. 107)</td>
<td>Spartin</td>
<td>AR Complex</td>
<td>Endosomal traffic, BMP signalling, Mitochondrial?</td>
</tr>
<tr>
<td>SPG21 (REF. 108)</td>
<td>Maspardin</td>
<td>AR Complex</td>
<td>Endosomal traffic</td>
</tr>
<tr>
<td>SPG31 (also known as REEP1)</td>
<td>REEP1</td>
<td>AD Pure</td>
<td>ER morphogenesis</td>
</tr>
<tr>
<td><strong>Mitochondrial</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG13 (also known as HSPD1)</td>
<td>HSP60</td>
<td>AD Pure</td>
<td>Mitochondrial chaperone</td>
</tr>
<tr>
<td>SPG7 (REF. 111)</td>
<td>Paraplegin</td>
<td>AR Complex</td>
<td>Mitochondrial protease</td>
</tr>
<tr>
<td><strong>Myelination</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG2 (also known as PLP1)</td>
<td>PLP</td>
<td>XLR Complex</td>
<td>Myelin protein</td>
</tr>
<tr>
<td>SPG35 (also known as FA2H)</td>
<td>Fatty acid 2-hydroxylase</td>
<td>AR Complex</td>
<td>Hydroxylation of myelin lipids</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPG1 (also known as L1CAM)</td>
<td>L1CAM</td>
<td>XLR Complex</td>
<td>Cell adhesion and signalling</td>
</tr>
<tr>
<td>SPG5 (also known as CYP7B1)</td>
<td>CYP7B1</td>
<td>AR Pure</td>
<td>Cholesterol metabolism</td>
</tr>
<tr>
<td>SPG30 (REF. 117)</td>
<td>Neuropathy target esterase</td>
<td>AR Complex</td>
<td>Phospholipid homeostasis, Target of organophosphates</td>
</tr>
<tr>
<td>SPG42 (also known as SLC33A1)</td>
<td>SLC33A1</td>
<td>AD Pure</td>
<td>Acetyl-CoA transporter</td>
</tr>
<tr>
<td>SPG48 (also known as KIAA0415)</td>
<td>KIAA0415</td>
<td>AR Complex</td>
<td>DNA repair</td>
</tr>
</tbody>
</table>

AD, autosomal dominant; AR, autosomal recessive; BMP, bone morphogenetic protein; CYP7B1, 25-hydroxycholesterol 7-alpha-hydroxylase; ER, endoplasmic reticulum; FA2H, fatty acid 2-hydroxylase; HSP60, heat shock protein 60; KIF5A, kinesin heavy chain isoform 5A; L1CAM, neural cell adhesion molecule L1; NIPA1, non imprinted in Prader-Willi/Angelman syndrome 1; PLP, myelin proteolipid protein; REEP1, receptor expression-enhancing protein 1; SPO, spastic paraplegia; SLC33A1, solute carrier family 33 (sodium/proton antiporter, member 1); XI, X-linked recessive.
Case 5: A Malady Of Movement
Diagnosis?
Differential Diagnosis

- Paroxysmal disorders
- Benign hereditary chorea
- Autoimmune
- Infectious/post infectious
- Structural: vascular, neoplastic
- Neurodegenerative
- Drugs
- Pregnancy
Chorea

• Abnormal involuntary movement derived from the Greek word “dance”.

• Brief, abrupt, irregular, unpredictable, non-stereotyped jerky movements
  - extremely fidgety, clumsy, uncoordinated and awkward
  - appear to be “making faces”

• Most often affects the face, arms, and hands
• Abnormal behavioral or emotional problems
• Exacerbated by stress, fatigue or excitement
• May only affect one side of the body
• Treatment: benzodiazepines, valproic acid, pimozide, tetrabenazine, corticosteroids, IVIG, and plasma exchange
Sydenham Chorea

- “St. Vitas Dance”
- Usually develops following Streptococcal infection
- Major complication of acute rheumatic fever
- Considered an autoimmune disorder
• Usual age of affliction is 5 -15 years
• More prevalent in girls than in boys
• Named for the 17th century English physician, Thomas Sydenham

Thomas Sydenham MD 1624 -1689
St. Vitus Dance
(Sydenham's Chorea, Infectious Chorea)

• The medieval name given to Sydenham chorea
• In the late Middle Ages people in Germany celebrated the feast of Vitus by dancing before his statue
• St. Vitus often invoked to alleviate the suffering of people with epilepsy
• Patron saint of dancing, epilepsy and actors
History

- 8 year old girl initially evaluated at 4 years of age for isolated motor developmental delay, abnormality of gait and abnormal movements
- Abnormal movements:
Abnormal Movements

• Initially ataxic and choreo-athetoid in nature
• Over time have become more overtly choreiform in nature with less prominent ataxia
• Remains very hyperkinetic
• Occasional dystonic posturing
• More recently - myoclonic jerks with sudden "give way" of her legs with falling
Examination

- No regression
- Examination is significant for hyperkinetic, involuntary, random choreiform movements, and unusual and unsteady gait with a mildly ataxic quality and areflexia
- Flexor plantar responses, normal cognition and strength
- No cerebellar signs
Diagnosis?
Differential Diagnosis

- **Ataxia telangetasia**
  - no clinical evidence and her immunoglobulins and AFP are normal
- **Rheumatic fever**
  - echocardiogram normal and she does not have any murmur or other features to suggest post rheumatic fever chorea
- **Celiac disease**: antibodies negative
- **Basal ganglia structural lesion**: MRI normal
Benign Hereditary Chorea

- Rare autosomal recessive childhood-onset movement disorder characterized predominantly by non-progressive chorea that tends to improve in adulthood
- Caused by mutations to the NKX2.1 gene
**NKX2.1 gene**

- *NKX2.1* gene is essential for organogenesis of the basal ganglia, thyroid and lungs.
- Clinical spectrum of patients with *NKX2-1* mutations:
  - Complete triad of brain–lung–thyroid syndrome (50%), brain and thyroid disease (30%) to isolated BHC (13%)

Chorea

- Chorea often generalized, affecting all body parts (face, limbs, trunk)
- Tends to worsen with stress or excitement
- Chorea often improves with time
- Myoclonus persists or worsens in some cases
• Normal intellect, but may have learning and behavior problems
• Other signs and symptoms may include thyroid problems (e.g., hypothyroidism) and lung disease (e.g., RDS, recurring infections, ILD)
• Treatment includes Tetrabenazine and levodopa
**NKX2.1 Gene Mutation**

- Other types of movement disorder also reported in *NKX2.1* mutation - either in isolation or in conjunction with chorea
- Includes ataxia, upper limb intention tremor, myoclonus, limb dystonia, and motor and vocal tics
Case 6: A Panoply of Problems
History

• 16 year old boy referred for second opinion for evaluation of possible Marfan syndrome or hypermobile Ehlers-Danlos syndrome
Signs and Symptoms

- Joint laxity, pes planus, hypermobility;
- Kyphosis and scoliosis
- Chronic daily headaches since age 8
- Droopiness of the right > left eyelid since middle school
- Intermittent hand tremors
- Anxiety
Evaluation

• Saw medical genetics x 2, orthopedic surgery x 2, neurologist x 2
• Echocardiogram normal
• Metabolic and genetic testing - normal
• Not felt to meet clinical criteria for a connective tissue disease
Examination

- Large size, stria on the back
- Mild pectus excavatum with mild gynecomastia.
- Right rib hump and prominent thoracic kyphosis with mild thoracic scoliosis
- Bilateral pes planus foot deformities
Neurological Examination

- Ptosis, right > left with no fatigability with sustained upgaze. Extra-ocular movements are full
- Hypotonic with hyper extensibility of elbows, wrists and fingers
- Strength, sensation, DTRs normal
Differential Diagnosis?
Differential Diagnosis?

- Cerebral gigantism
  - Pituitary adenoma
  - Sotos syndrome (*NSD1* gene mutation)
- Acromegaly
- Weaver syndrome (*EZH2* gene mutation)
- Carney complex (*PRKAR1A* gene mutation)
- McCune-Albright syndrome (*GNAS1* gene mutation)
- Beckwith-Weidemann syndrome
Diagnosis ?
Gigantism Secondary to Pituitary Macroadenoma (with right cavernous invasion)
Gigantism versus Acromegaly

- Gigantism refers to abnormally high linear growth due to excessive action of insulin-like growth factor I (IGF-I) while the epiphyseal growth plates are open during childhood.
- Acromegaly is the same disorder of IGF-I excess but occurs after the growth plate cartilage fuses in adulthood.
Case 7: A Sad Tale
History

- 7 year old boy with Lowe’s syndrome, mild developmental delays and learning difficulties
- Presents with a week of paroxysmal spells described as “grabbing his head and screaming” lasting for about a minute each, several times a day
- In between the spells, mother describes him as slow and uncoordinated.
Birth and Development

- Born at 29 weeks gestation
- Prenatal diagnosis of Lowe’s syndrome
- NICU stay ~ 2.5 months.
- Started walking at ~ 2 years of age
- First words were at 2.5 years, 2 words ~ 3 years
Diagnosis: Complex Partial Epilepsy

- Spells confirmed to be seizures arising from the left fronto-temporal and right centro-parietal-temporal region
- Started on Oxcarbamazepine with resolution of screaming spells
Oculocerebrorenal Syndrome of Lowe

- Vision problems including cataracts that are present at birth; glaucoma
- Kidney problems usually develop in the first year of life (Fanconi syndrome)
- Brain abnormalities that are associated with intellectual disabilities; seizures
- Lowe syndrome is inherited as an X-linked genetic condition.
Case 8: In The Eyes Of The Beholder
History

• 15 year old boy initially seen for problems of hypotonia as an infant
• Also problems with early mild developmental delay and some persistent academic and coordination difficulties when older
• Birth and family history non-contributory
• Past medical history otherwise unremarkable
Diagnosis?
Duane Syndrome

- A congenital non-progressive eye movement disorder
  - prevalence 1:1000
  - Slightly more common in females (3:2 ratio)
- Characterized by:
  - Limitation of abduction and/or adduction
  - Globe retraction on adduction of eye
  - Palpebral fissure narrowing on adduction of eye
- Most cases (70%) are isolated with no other congenital anomalies
- Rarely familial – associated with mutations in the CHN1 gene
Pathophysiology

• Results from maldevelopment of motor neurons in the abducens nucleus and aberrant innervation of the lateral rectus muscle by branches from the oculomotor nerve

• Simultaneous activation of the medial and lateral rectus muscles cause of the globe retraction
Case 9: A Wry Smile
History

- Asked to see this newborn baby for abnormal facial appearance
- Normal antenatal course, labor, and delivery
- Apgars 9 and 9
- No resuscitation; no instrumentation
Diagnosis?
Cayler Cardiofacial Syndrome

- Congenital absence or hypoplasia of the angularis oris muscle
  - Innovated by ramus marginalis mandibulae
- Possible autosomal dominant inheritance
  - Higher incidence of 22q11 microdeletions
- Congenital heart disease (44%)
- Central nervous system (10%)
  - Microcephaly, MR
  - Cerebral and cerebellar atrophy
- 0.5 -1% of newborns
Cleveland Clinic

Every life deserves world class care.