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Disclosures

- No financial disclosures

- My opinions
  - Based on experience and literature

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Defining Ataxia

- From the Greek “a taxis”
  - Lack of order
- Disturbance in fine control of posture and movement
- Can result from cerebellar, sensory or vestibular problems
Defining Ataxia

- Not attributable to weakness or involuntary movements:
  - Chorea, dystonia, myoclonus, tremor
  - Distinguish between ataxic and “clumsy”

- From impairment of one or both:
  - Spatial pattern of muscle activity
  - Timing of muscle activity
Brainstem anatomy

[Diagram showing brainstem anatomy with labeled parts such as Corpus Callosum, Septum Pellucidum, Fornix, Third ventricle, Pons, Optic chiasma, Cisterna interpeduncularis, Fourth ventricle, Cisterna pontis, Medulla oblongata, Cisterna cerebellomedullaris, and Cerebellum.]
Cerebellar function/Ataxia

- Vestibulocerebellum (flocculonodular lobe)
  - Balance, reflexive head/eye movements
- Spinocerebellum (vermis, paravermis)
  - Posture and limb movements
- Cerebrocerebellum
  - Movement planning and motor learning
Cerebellar Anatomy (Function)

- **Spino-cerebellum**
  - Regulates muscle tone and coordination of skilled voluntary movement.

- **Cerebro-cerebellum**
  - Involved in planning and modulation of voluntary activity, storage of procedural memories.

- **Vestibulocerebellum**
  - Maintains balance and control of eye movements.
Vestibulocerellum - Archicerebellum

- Abnormal gate
  - Abasia - wide based, lurching, staggering
  - Alcohol impairs cerebellum
- Titubations –
  - Trunk/head tremor - Vermis lesions
- Tandem gait
  - Fall or deviate toward lesion - Hemisphere lesions
Vestibulocerebellum

- Ocular dysmetria
  - Saccades over/undershoot target
  - Jerky saccadic movements during smooth pursuit
- Nystagmus with peripheral gaze
  - Slow toward primary, fast toward target
  - Horizontal or vertical
  - May change direction
  - Does not extinguish with fixation
- Impaired suppression of VOR
Spinocerebellum - *Paleocerebellum*

- **Dysmetria**
  - Over/undershoot, past-pointing
- **Dysrhythmia/Asynergia**
  - Decomposition of complex movements
- **Dysdiadochokinesis**
  - Impaired rate/regularity of alternating movements
- **Tremor**
  - Intention/action - during movement toward target
- **Impaired check/excessive rebound**
Cerebrocerebellum - Neocerebellum

- Speech - Articulation and prosody
  - Scanning or explosive
    - Irregular fluctuations rate and volume
  - Dysarthria
    - Slurred Speech – extreme = mutism
- Limb ataxia
- Hypotonia
- Intention tremor
- Cognitive affective syndrome
Cerebellar Anatomy (Lobes)

Anterior lobe – input from spinal cord
Posterior lobe – input from cerebrocorticol via pons
Flocculonodular lobe – input from vestibular
Humunculus

- Cerebellum
- Vermis
- Anterior Lobe
- Posterior Lobe
- Floccular Lobe (balance)
Cerebellar Peduncles

- Corticopontine fibers
- Pons
- Pontine mossy fibers
- Middle cerebellar peduncle
- To thalamus and red nucleus
- Superior cerebellar peduncle
- Cerebellum
- To vestibular nuclei
- Interposed
- Fastigial
- Inferior cerebellar peduncle
- Climbing fibers from inferior olive
- Proprioceptive information from spinocerebellar tract (mossy fibers)
Cerebellar Connections

Cerebellum integrates motor information

- Thalamus
- Basal nuclei
- Sensory input
- Brainstem
- Spinal cord
- Cortex
Cerebellar Blood Supply

SCA
AICA
Basilar
Vertebrals
PICA
Cerebellar Anatomy - Micro
Sensory Ataxia

- Loss of sensory input to cerebellum
  - Peripheral nerve or posterior column
  - DM, syphilis, B12 deficiency, etc
- Looking at feet
- Wide-based and careful gate
  - Foot raised high, slaps with each step
- Worse with eyes closed or in a dark room
  - Romberg: vision, proprioception, vestibular
- Difficulty w/fine finger movements
  - Rather than reaching for objects
Vestibular Ataxia

- Acute vestibular neuronitis
  - Postinfections
    - URI/prodrome
  - Adolescents/adults
  - Acute dysequalibrium, peripheral nystagmus
  - Preserved auditory function

- Labyrinthitis
  - Tinnitus, SN hearing loss
  - Vertigo, vomiting, pallor, sweatiness
  - Nystagmus (even with eyes closed)
Ataxia

- Acute or recurrent vs. chronic or progressive

- May confuse acute with a progressive that ‘suddenly’ become apparent

- Today – cover acute
  - Some recurrent – brief mention
  - Chronic/progressive – NEXT TIME?
Most Common Causes

- Two Most Common
  - Drug ingestion
  - Acute postinfectious cerebellitis

- Most cost effective test:
  - Drug screen

- Most important test:
  - Good neurological exam (including fundoscopic)
Drug Ingestion

CAUSES OF ATAXIA
Drug Ingestion

- One of the most common causes of acute ataxia in previously well children
  - Highest rate of accidental ingestion
    - 1-4 years of age
  - Intentional overdose or abuse
    - Teenagers
Drug Ingestion
Clinical Features (ataxia +)

- Psychoactive drugs
  - Alcohol, benzos, narcotics, stimulants, THC
  - Change in personality and sensorium and occas sz

- Anticonvulsants (Phenytoin)
  - Nystagmus and ataxia w/o change in sensorium

- Antihistamines
  - Especially if child has otitis media
Drug Ingestion
Diagnosis and Management

- Question care providers, family, friends
- Urine and blood screening
- Supportive treatment
- Can usually be safely eliminated spontaneously
  - Charcoal, lavage, reversal agents
- Might require dialysis if life threatening
Brain Tumor

CAUSES OF ATAXIA
Brain Tumor

- Usually chronic progressive
- Acute if bleeds or causes hydrocephalus
- Early clumsiness may not be initially apparent
- Nighttime HA w/ vomiting
- Exam:
  - Papilledema
  - Head tilt
  - 6th nerve palsies
  - Stiff neck or torticollis
Brain Tumors

- 85% primary brain tumors 2-12 yo
  - Located posterior fossa
- 4 major types:
  - *Cerebellar astrocytoma
  - Brainstem glioma
  - *Ependymoma
  - Primitive neuroectodermal tumor
    - *Medulloblastoma
- Up to 25% supratentorial tumors - ataxia
Pilocytic Astrocytoma
Brainstem Glioma
Ependymoma
Medulloblastoma
Conversion Reaction

CAUSES OF ATAXIA
Conversion Reaction

- Relatively common in children
- Girls > boys 10-15 years of age
- Involuntary (not faking)
- Sits w/o difficulty
  - Immediately sways from waist when stands
  - Stance is not wide based
  - Lurch around room
    - Often complex, requiring incredible balance
Conversion Reaction

- Diagnosis by observation
  - Astasia-abasia
  - Other: Splitting middle, vibration/proprioception, Hoover/ give away weakness/abnl drift, mixed/crossed patterns, La belle indifference, unusual complaints

- Treatment
  - Determine precipitating stress

- Conversion may be cry for help
  - ie: Sexual Abuse - require multi-specialty team

- Münchausen syndrome – not involuntary
  - More obvious secondary gain, more difficult to treat
Migraine

CAUSES OF ATAXIA
Basilar Migraine

- Brainstem or cerebellar dysfunction
  - Recurrent
  - FH of classical or complex migraine

- Girls > boys

- Peaks during adolescence
  - Infant onset more likely present as
    - Benign paroxysmal vertigo
Basilar Migraine

Clinical Features

- Gait ataxia - 50%
- Visual loss
- Vertigo
- Tinnitus
- Alternating hemiparesis
- Paresthesias- fingers, toes, corner of mouth
- Cranial nerve palsies
- Seizure
Basilar Migraine
Clinical Features

- Abrupt loss of consciousness
  - Usually only lasts a few minutes

- Cardiac arrhythmias, brainstem stroke
  - Rare but life-threatening

- Severe throbbing occipital HA follows

- Nausea/vomiting in less than 1/3
Basilar Migraine

- May have repeated attacks

- With time, evolve into classic migraines
  - Might still c/o vertigo and/or ataxia

- FH of complex or classical migraines
Basilar Migraine
Diagnosis

- EEG to distinguish from occipital epilepsy
  - Basilar Migraine Findings
    - Occipital intermittent delta activity during and after an attack
  - Occipital Epilepsy
    - Occipital discharges

- MRI brain with MRA at first presentation
- Prophylactic meds to prevent
Benign Paroxysmal Vertigo

CAUSES OF ATAXIA

MIGRAINE
Benign Paroxysmal Vertigo

- Migraine variant in children
- Primarily infants and preschool children
  - Can occur in older children
- Episodes last minutes
- Recur with irregular intervals
- Over time, decrease in frequency then stop
- May develop migraines in later life
Benign Paroxysmal Vertigo
Clinical Features

- Vertigo is maximal at onset
- Pallor, nystagmus, fright
- Not true cerebellar ataxia
  - Vertigo makes standing impossible
- Child lies motionless or want to be held
- Consciousness is maintained
- No headache
- Resolves with sleep
Benign Paroxysmal Vertigo
Diagnosis and Treatment

- Family history of migraine in 40%
  - Rarely paroxysmal vertigo

- Some parents have vertigo w/migraines

- Brief, no treatment required
Infectious

CAUSES OF ATAXIA
Cerebellar Abscess

- Often spread from otitis media or mastoiditis
- Ataxia and fever
- Mass effect
  - HA and vomiting
- Can rupture into subarachnoid space
  - Rapid deterioration - death
  - Meningismus
Cerebellar Abscess
POSTINFECTIOUS/AUTOIMMUNE DISORDERS
Postinfectious/Autoimmune Disorders

- Altered immune state leads to neurological dysfunction
  - Cross-reactivity between host and infectious antigens

- Preceding viral illness likely
  - Documented in <½ of cases
  - ?Cause and effect

- Variety of antibodies associated
  - ?Cause and effect
Postinfectious/Autoimmune Disorders

- Acute Cerebellar Ataxia
- Acute Disseminated Encephalomyelitis (ADEM)
- Guillain-Barré Syndrome
  - Bickerstaff's Brainstem Encephalitis
  - Miller Fisher Syndrome
- Multiple Sclerosis
- Opsoclonus-Myoclonus (Neuroblastoma)
Acute Cerebellar Ataxia
(Acute Cerebellitis)

POSTINFECTIONOUS/
AUTOIMMUNE DISORDERS
Acute Cerebellar Ataxia

- Usually children 2-4 years of age
  - Can occur at any age, but rare after adolescence
- No known genetic predisposition, M=F
- Classically after VZV infection > vaccine
  - Virtually every infection has been reported
- Can occur days to months after infection
  - Typically 7-10 days
  - 20% no prodrome/infection
Acute Cerebellar Ataxia
Clinical Features

- Ataxia - Explosive and maximal at onset
  - Truncal > extremity
  - Titubation, tremor, dysmetria
  - All have severe impairment of gait

- May awake from nap unable to walk

- Some worsening may occur initially (hours)
  - Longer progression or waxing/waning

- Not acutely ill appearing
  - Can still have VZV rash
Acute Cerebellar Ataxia
Clinical Features

- Reflexes present or absent
  - Absent – consider Miller Fisher Syndrome

- Nystagmus mild if present
  - Opsoclonus – consider opsoclonus-myoclonus

- Sensorium clear, otherwise well appearing
  - May have mutism or severe dysarthria
  - Altered mental status
    - Encephalitis
    - Meningitis
    - Seizure
    - Hemorrhage
Acute Cerebellar Ataxia
Clinical Features

- Symptoms begin to improve after a few days
- Gait takes 3 weeks to 5 months to normalize
- Transient behavioral problems – 20%
- Complete recovery in most – 90%
- Persistent neurological sequelae rare
  - Marked nystagmus/opsoclonus, tremors of head and trunk, moderate irritability, learning disabilities
Acute Cerebellar Ataxia Diagnosis and Treatment

- Diagnosis of exclusion
  - Admit for observation at minimum
- Drug screen, brain imaging
  - Debatable in patients with varicella infection
  - Imaging usually normal
- LP if encephalitis is suspected (after imaging)
  - Non-specific pleocytosis, oligoclonal bands
- Variety of autoantibodies reported
  - Not commercially available
Acute Cerebellar Ataxia
Diagnosis and Treatment

- Self-limited, no treatment required
  - Symptomatic treatment

- **Life-threatening progression can occur**
  - Cerebellar herniation with brainstem compression
  - IVIG, steroids, antivirals, plasmapharesis?
  - Posterior decompression, VP shunt
    - May be fatal despite all interventions
    - Case reports only, nothing predictive of progression
Acute Cerebellitis
Acute Cerebellitis - acute vs after recovery
Guillain-Barré Syndrome (AIDP)

POSTINFECTIOUS/ AUTOIMMUNE DISORDERS
Guillain-Barré Syndrome
Clinical Features

- Acute inflammatory demyelinating polyradiculopathy
- Presumed post-infectious and immune mediated
- Predominantly affects motor nerves
  - Progressive ascending weakness, areflexia
  - May have sensory ataxia or appear ataxic due to weakness
  - Cytoalbuminic disassociation (elevated protein) – initially nl
  - Enhancing nerve roots on lumbosacral MRI
- Majority of children have full recovery (months)
- Treat w/ IVIG or plasmapheresis vs supportive
Miller Fisher Syndrome/Variant

POSTINFECTIOUS/AUTOIMMUNE DISORDERS
Miller Fisher Syndrome

- Ataxia
- Areflexia
- Ophthalmoplegia
  - No ophthalmoplegia -> Acute sensory ataxic neuropathy
- Guillain-Barre syndrome vs a form of brainstem encephalitis
Miller Fisher Syndrome
Clinical Features

- 50% with preceding viral illness
  - Precedes by 5-10 days

- Initially with ophthalmoparesis or ataxia
- Often have no or mild weakness

- Recovery begins within 2-4 weeks
  - After symptoms become maximal

- Complete recovery within 6 months
  - Better prognosis
Miller Fisher Syndrome
Clinical Features

- Ocular motor disturbance
  - Paralysis of upgaze, then lateral, then down gaze
  - Ptosis occurs also
  - Recovery in reverse

- Areflexia
  - Likely due to decreased peripheral sensory input

- Ataxia
  - More prominent in limbs than trunk
Miller Fisher Syndrome
Diagnosis and Treatment

- CSF
  - Early cellular response
  - Later protein elevation
  - Parallels Guillain-Barré
  - Anti GQ1b Ab (targets Schwann cells)

- Distinguished from brainstem encephalitis by:
  - No change in sensorium, CN palsies, EEG changes, prolonged interpeak latency on BAER.

- Treatment
  - IVIG, plasmapharesis
Bickerstaff's Brainstem
Encephalitis

POSTINFECTIOUS/AUTOIMMUNE DISORDERS
Brainstem Encephalitis

- Viral encephalitis
  - Affecting posterior fossa
  - Ataxia may be initial feature

- Potential etiologic agents
  - Viral, bacterial, vaccine
    - Like GBS, MFS, and ACA
Brainstem Encephalitis

- Ataxia + cranial nerve dysfunction
- Declining consciousness and sz
- Hyperreflexia vs areflexia
- Sometimes with meningismus
Brainstem Encephalitis

- Variable Course
  - Most recover completely
  - Best prognosis if only ataxia and CN involvement
    - Overlap clinically with Miller Fisher Syndrome
  - Some have considerable impairment
    - Can be fatal
  - Worse prognosis if paraneoplastic
Brainstem Encephalitis Diagnosis

- CSF cellular response required
  - Primarily mononuclear leukocytes
  - With or w/o elevated protein

- BAER- brainstem auditory evoked responses
  - Prolonged interpeak latencies
  - Evidence of brainstem parenchymal abnormality

- EEG usually normal if normal sensorium
Brainstem Encephalitis
Treatment

- Supportive
- ? IVIG, plasmapheresis, steroids
- Physical therapy
Brainstem Encephalitis
Acute Disseminated Encephalomyelitis (ADEM)
ADEM

- Inflammatory demyelinating disease
  - Affects brain and spinal cord
  - Affects grey and white matter

- Uncommon, usually occurs in children

- Usually follows an infection vs vaccination

- May have ataxia as part of presentation
ADEM

Clinical Features

- Fever, headache, fatigue initially
- Confusion progressing to stupor or coma
- Seizures
- Cranial neuropathies
- Weakness
- Hemiparesis
- Sensory deficits
- Hyperreflexia
- Vision loss (optic neuritis)
- Paralysis w/ sensory level (transverse myelitis)
ADEM

- Most patients recover slowly (months)
- ~2/3 without neurologic deficit
- Up to a 5% mortality rate
- Up to 25% may go on to have MS
  - Rarely recurs
ADEM
Diagnosis

- CSF
  - Pleocytosis common (mild)
  - Open pressure may be increased or normal
  - Negative or transient OCBs, elevated MBP

- MRI
  - Asymmetric, multifocal T2 hyperintensities
  - Involves white and grey matter
    - Spares periventricular white matter
  - All lesions acute and usually resolve
ADEM – Lesions resolve

Onset

8 weeks later
ADEM – Longitudinal TM
MRI – Grey and White Matter
ADEM – Ring Enhancement
ADEM
Treatment

- No standard of care
  - Steroids
  - IVIG or Plasmapharesis
  - Supportive

- Unclear if treatment affects outcome

- Follow-up imaging warranted
  - Ensure resolution
  - Ensure no new lesions
Multiple Sclerosis

POSTINFECTIOUS/ AUTOIMMUNE DISORDERS
Multiple Sclerosis

- 3-5% of cases occur in children under 16 years of age

- Repeated episodes of demyelination in noncontiguous areas of CNS.

- Clinically variable presentation
Multiple Sclerosis

- Focal neurological deficits develop rapidly and persist for weeks to months
- Months or years between recurrences
  - Often concurrent with febrile illness
- Longterm outcome unpredictable
Multiple Sclerosis
Clinical Features

- Ataxia - truncal and limb
  - Most common initial feature

- Behavior changes

- Neurocognitive difficulties

- Fatigue

- 1/3 with internuclear ophthalmoplegia (INO)
  - Unilateral or bilateral
Right INO
Oculomotor circuitry - MLF
Multiple Sclerosis
Clinical Features

- Lethargy, nausea and vomiting more common than with adults
- Paresthesias or pain
- Bowel/bladder problems
- Hemiparesis
- Seizures
- Irritability in young children
- Reflexes brisk or normal
Multiple Sclerosis Diagnosis

- Dissemination in time
  - Recurrent attacks – ADEM/optic neuritis initially
  - New lesions on MRI – may be asymptomatic
  - Enhancing (new) and non-enhancing (old)
    - Initial MRI

- Dissemination in space
  - Multiple lesions, or specific locations
  - Abnormal CSF – oligoclonals, MBP
  - Abnormal VEP, BAER, SSEP
Multiple Sclerosis Treatment

- Treatment
  - Acute
    - Short course IV steroids
  - Recurrence
    - IV steroids
  - Resistant
    - IVIG, plasmapharesis
  - Prevention
    - Interferons, glatiramer acetate
      - Tysabri - monoclonal Ab - PML
ADEM vs MS
Dawson’s Fingers
MS- MRI
Contrast Enhancement
Opsoclonus-Myoclonus Syndrome

POSTINFECTIOUS/AUTOIMMUNE DISORDERS
Opsoclonus-Myoclonus Syndrome

- Chaotic eye movements
  - Dancing eyes, opsoclonus

- Myoclonic ataxia

- Encephalopathy

- Not all cases related to neuroblastoma
  - Postinfectious

- 2-3% of children with neuroblastoma develop
Opsoclonus-Myoclonus Syndrome
Clinical Features

- Onset 1 month to 4 years
  - Peak incidence 18-24 months

- Evolution of symptoms takes >= 1 week

- Ataxia/opsoclonus brings patient in

- ½ with Personality change or irritability
  - Diffuse encephalopathy
Opsoclonus-Myoclonus Syndrome
Clinical Features

- **Myoclonus**
  - Imbalance not due to ataxia
  - Constant rapid muscle contractions
  - Irregular, widespread occurrence

- **Opsoclonus**
  - Spontaneous, conjugate, irregular jerking
  - All directions
  - Worse when trying to change fixation
  - Blinking or eyelid flutter
  - Persists in sleep, worse with agitation
Opsoclonus-Myoclonus Syndrome

Clinical Course

- Often a prolonged course
- Waxing/waning vs remission
- Often misdiagnosed initially as ACA
- Symptoms paraneoplastic
  - Removal of tumor DOES NOT affect symptoms
Opsoclonus-Myoclonus Syndrome

Diagnosis

- Clinical features

- Look for the Neuroblastoma
  - MRI of chest and abdomen
  - Urinary homovanillic (HVA) and vanillylmandelic (VMA) acids
  - **MIBG scintiscan

- Equal likelihood neuroblastoma
  - Chest or abdomen
    - More common in abdomen w/o OM
Opsoclonus-Myoclonus Syndrome

Treatment

- **Medical**
  - **ACTH**
  - Pulse dose steroids
  - IVIg, plasmapheresis, B-cell monoclonal
  - 80% get partial or complete relief

- **Marked improvement**
  - 1-4 weeks with treatment

- **Relapses can occur after or during treatment**

- **neurological deficits long term**
  - 2/3 patients - mild
Pseudoataxia
(Epileptic Ataxia)

CAUSES OF ATAXIA
Pseudoataxia
Clinical Features

- Gate disturbance may be seizure
- Limb and gait ataxia
- Sudden in onset and episodic
- May appear inattentive or confused
- If on AED, could be toxicity
  - Should see nystagmus
Pseudoataxia
Diagnosis and Treatment

- EEG
  - Prolonged, generalized 2-3Hz spike-wave complexes with frontal predominance
  - Typical for Lennox-Gastaut
    - Myoclonic jerks or akinetic seizures can disrupt smooth movement

- Nystagmus suggests AED toxicity
- Treat with AED
- Can also be post-ictal phenomenon
CAUSES OF ATAXIA

Trauma
Trauma-Postconcussison Syndrome
Clinical Features

- HA, dizziness, mental changes

- Cerebral axonopathy
  - Even mild head trauma can cause ataxia
  - May explain persistent symptoms
Trauma-Postconcussion Syndrome
Clinical Features

- Infants and young children
  - Ataxia is most prominent symptom
  - Not cerebellar ataxia; just unsteady
  - No limb dysmetria/other neuro abnormality
Trauma-Postconcussion Syndrome
Clinical Features

- Older children
  - Ataxia, HA and dizziness/vertigo are equally common
  - HA usually low grade/constant
    - Often analgesic rebound HA
  - Gate is less disturbed
    - Sensation of unsteadiness is still present
Trauma-Post-Concussion Syndrome
Diagnosis and Treatment

- Clinically diagnosed

- CT to exclude hemorrhage – if AMS/LOC

- MRI may show foci of T2 hyper-intensity
  - Diffuse axonal injury (DAI)

- Decreased activity during ataxia
  - Usually resolves within 1 month
  - Can last up to 6 months
Trauma- Vertebrobasilar Occlusion

- Vertebral arteries from C2 to foramen magnum
  - Encased by bony canal
  - Hyperflexion or extension
  - Endothelial injury and thrombosis

- May occur with chiropractic manipulation - rare

- Sports injuries
Trauma - VBO

Clinical Features

- Onset within minutes to hours of injury

- Vertigo, nausea, vomiting, +/- occipital headache
  - Brainstem ischemia

- Ataxia
  - Due to incoordination of limbs on one side
  - Maximal at onset or progressive over several days

- Unilateral brainstem disturbance
  - Diplopia, facial weakness

- Ipsilateral cerebellar dysfunction
Trauma- VBO
Diagnosis and Treatment

- CT or MRI
  - Unilateral cerebellar hemisphere infarct
  - May infarct lateral medulla

- Arteriogram
  - Localizes the thrombosis

- Many children recover within months
  - IA tPA in several case reports but little on anticoagulation
Posterior Circulation Anatomy
Occlusion/Stroke
Vascular Disorders

CAUSES OF ATAXIA
Vascular Disorders: Cerebellar Hemorrhage

- Spontaneous Cerebellar Hemorrhage
  - Coagulopathy
  - AV malformation
    - <10% of intracranial AVMs are cerebellar

- Ataxia and headache
- Can rapidly become fatal
  - Brainstem compression – apnea
- Urgent neurosurgery eval, admit PICU
Cerebellar Hemorrhage
Vascular Disorders: Vasculitis

- Uncommon cause of ataxia
  - Predominantly in infants and children
- More likely to present with:
  - Seizures
  - Alterations in consciousness
  - Stroke
  - Behavior changes
- Kawasaki’s, SLE, HSP, etc all reported
CAUSES OF ACUTE ATAXIA

Others
Others

- Tick paralysis
- Hypoglycemia
- Metabolic disorders
- Posterior fossa congenital anomalies
  - May present acute as child begins to reach milestones

- Is the child really ataxic?
Nonprogressive Ataxia
Clumsy Child

- Often associated with:
  - Mild GM/FM delays
  - Speech articulation difficulties
  - Learning disabilities, ADHD, other

- Static process, no regression

- Mild incoordination and hypotonia
Clumsy Child

- Defer w/u unless:
  - Syndromic/dysmorphic
  - Macro/microcephaly
  - GDD
  - Abnl neuro exam
    - Brain MRI, Fragile X, CGH, High Res Chromosomes

- OT/PT/ST, f/u
  - Ensure improvement, no regression
Nonprogressive Ataxia - Congenital

- Dandy-Walker malformation
  - Core features:
    - Partial or complete agenesis cerebellar vermis
      - Elevated and upwardly rotated
    - Cyst-like dilatation of the fourth ventricle
  - Other features often present:
    - Hydrocephalus
    - Enlargement of the posterior fossa
    - Elevation of the tentorium, transverse sinus, or both
    - Lack of patency foramina of Luschka and/or Magendie
Dandy-Walker Malformation
Nonprogressive Ataxia - Congenital

- Joubert’s syndrome
  - Vermis agenesis
  - Dysplasia and heterotopias of cerebellar nuclei
  - Superior cerebellar peduncle elongation
  - Brainstem anomalies
  - **Hyperpnea, apnea, MR, ataxia, abnl eye mvmts**
  - 10+ gene mutations – cilia proteins
  - AR > XL
Joubert’s Syndrome

Fig 2 (A and B). MRI showed posterior cerebellar vermis hypoplasia and “molar tooth appearance”
Nonprogressive Ataxia - Congenital

- Cerebellar/pontocerebellar hypoplasia
  - Smith-Lemli-Optiz
  - Bilateral periventricular nodular heterotopia/MR
  - Pontocerebellar hypoplasias
  - Congenital disorders of glycosylation
  - Bilateral cerebellar hypoplasia (>50% genetic)
  - Vermis hypoplasia (isolated vs nonspecific other CNS malformations)
Nonprogressive Ataxia – Cerebellar Atrophy

- Infant
  - Hypotonia, devel delay, abnl eye movements
- Toddler
  - Titubation, ataxia, intention tremor, dysmetria
- Outcome difficult to predict
  - No 1:1 correlation with MRI findings
  - Assoc anomalies, genetic abnl – more significant
Nonprogressive Ataxia - Congenital

- Basilar impression
  - Posterior odontoid displacement
  - Compresses spinal cord or brainstem

- Chiari Malformation
  - Downward displacement cerebellar tonsils through foramen magnum
  - Compresses spinomedullary junction

- **Can become symptomatic after minor CHI**
- Treated with posterior fossa decompression
Basilar Impression
Chiari Malformation
Chiari Malformation
Chiari Malformation
CAUSES OF ATAXIA

Genetic Disorders
Questions?
Episodic Ataxia Type 1 (Paroxysmal Ataxia and Myokymia)
Episodic Ataxia Type 1

- Mutation K⁺ Channel Gene KCNA1, Ch 12p13
- Onset between 5-7 years of age
- Myokymia starts around 12 years of age
- Triggered by:
  - Startle
  - Anxiety
  - Abrupt postural change or movements
  - Fevers
Episodic Ataxia Type 1

- Initial symptoms last a few seconds
  - Limpness or stiffness

- Attack lasts from less than 10 min to 6 hrs
  - Incoordination, head/limb trembling, blurred vision
  - Myokymia of face and limbs
  - Some children feel warm and perspire
  - Some can continue standing, most sit down
Episodic Ataxia Type 1
Clinical Features

- Large calves
- Normal muscle strength
- Widespread myokymia of face, hands, arms, legs
- Hand posture resembling carpopedal spasm
Episodic Ataxia Type 1
Diagnosis and Treatment

- EMG at rest shows continuous spontaneous activity

- Treat with acetazolamide
  - Phenytoin or Carbamazepine also options
Episodic Ataxia Type 2
(Acetazolamide-Responsive Ataxia)
Episodic Ataxia Type 2

- Chromosome 19p13  **CACNA1A**
  - Calcium channel

- Point mutations cause:
  - EA-2
  - Familial hemiplegic migraine

- Repeat expansions cause:
  - EA-2
  - One form of spinocerebellar ataxia (SCA 6)
Episodic Ataxia Type 2

- Clinically heterogeneous
- Onset generally school age or adolescence
- 1-3 attacks may occur per month
- Can last hours to days
- Attacks become milder and less frequent w/age

Triggers:
- Emotional upset
- Exercise
- Alcohol
- Caffeine
- Phenytoin
Episodic Ataxia Type 2

- Unsteadiness
- Vertigo and Ataxia
  - Inability to maintain posture
- Frequent and severe vomiting
- Nystagmus- gaze evoked, down beating
- Impaired VOR and saccades
Episodic Ataxia Type 2

- Between attacks
  - Truncal ataxia may progress
  - Nystagmus may persist

- Some patients only have
  - Ataxia, vertigo or nystagmus

- Most are normal between attacks

- Can be indistinguishable from SCA 6
  - Progressive hereditary ataxia with dystonia
Episodic Ataxia Type 2

Diagnosis

- Clinical features

- Family history

- MRI may show atrophy of cerebellar vermis

- EA-2 compared to Basilar artery migraine
  - Basilar migraine family members have migraines, not EA-2 sx

- EA-2 compared to BPV
  - BPV attacks usually < few minutes
Episodic Ataxia Type 2

- Treat with acetazolamide
- Prevents recurrence of attacks
- Flunarizine for acetazolamide intolerance
Hartnup Disease
Hartnup Disease

- Rare
- Autosomal recessive
- Chromosome 5p15
Hartnup Disease

- Defect of AA transport in kidney and SI
  - Aminoaciduria
  - AA retention in SI

- Tryptophan conversion
  - Non-essential indole products instead of nicotinamide
Hartnup Disease
Clinical Features

- Normal at birth
- Delayed developmental milestones
- Borderline to normal intelligence
- Photosensitive
  - Pellagra-like skin rash
  - Due to nicotinamide deficiency
Hartnup Disease
Clinical Features

- Limb and gait ataxia, tremor
- Nystagmus, diplopia
- Mental changes
  - Emotional instability
  - Delirium
  - Decreased consciousness
- Diarrhea
Hartnup Disease
Clinical Features

- Exam
  - Hypotonia
  - Normal to increased DTRs
  - Rash and neuro disturbances
    - Usually together; can be alone

- Triggers of neurologic changes
  - Stress-emotional or physical w/ poor nutrition
  - Intercurrent infections

- Symptoms progress over days, last for 1-4 weeks
Hartnup Disease
Diagnosis and Treatment

- Aminoaciduria - monoaminomonocarboxylic aa’s
  - Serum and urine amino acid panel

- Oral nicotinamide
  - May reverse skin and neuro complications

- High protein diet
  - Helps make up for amino acid loss
Maple Syrup Urine Disease
Maple Syrup Urine Disease

- Neonatal organic acidemia

- Branched-chain ketoacid dehydrogenase deficiency
  - Disorder of branched-chain AA metabolism
  - Organic acidemia

- Autosomal recessive
Phenotypes of MSUD

- 3 types (depends on amount of enzyme)
  - Classic
    - seizures in newborn
  - Intermediate
    - progressive MR
  - Intermittent
    - recurrent attacks of ataxia and encephalopathy
Intermittent MSUD (Ataxia)
Clinical Features

- Normal at birth
- Symptoms at 5mo to 2 yr of age

- Triggers
  - Minor infections
  - Surgery
  - Protein-rich diet
Intermittent MSUD
Clinical Features

- Ataxia
- Irritability
- Progressive lethargy
- Length of attacks vary
- Most recover spontaneously
- Metabolic acidosis can lead to death
- Survivors have normal development
Intermittent MSUD Diagnosis

- During attack
  - Maple syrup odor to urine
  - Urine and blood with increased branched-chain amino and keto acids
    - Normal btw attacks
    - Urine OAs, serum and urine AAs

- Diagnosis
  - Enzyme deficiency in cultured fibroblasts
Intermittent MSUD
Treatment

- Protein restricted diet

- Some are thiamine-responsive
  - Up to 1g/day for acute attacks
  - If successful -> daily maintenance dose

- Goal during acute attack
  - Reverse ketoacidosis
  - May need peritoneal dialysis
  - NO PROTEIN
Pyruvate Dehydrogenase Deficiency
PDH Deficiency

- **PDH Complex**
  - Oxidative decarboxylation of pyruvate
    - To carbon dioxide and acetyl coenzyme A
  - Required for Krebs cycle

- Disorders associated with several neurological conditions
  - Leigh disease
  - Mitochondrial myopathies
  - Lactic acidosis
PDH Deficiency

- Complex contains 3 main components
  - E1, E2, and E3
  - E1 has 4 subunits
    - 2 alpha subunits coded from X and 2 beta subunits

- X-linked form of PDH-E1 deficiency
  - The most common form of PDH deficiency
  - Intermittent ataxia and lactic acidosis
PDH Deficiency
Clinical Features

- Wide range of manifestations
- Severe neonatal lactic acidosis and death
- Episodic ataxia with
  - Elevated lactate and pyruvate
  - Spinocerebellar degeneration
PDH Deficiency
Clinical Features

- **Infancy**
  - More severely affected patients
  - Generalized weakness and states of decreased consciousness

- **Early childhood**
  - Most with mild developmental delay

- **After 3 years of age**
  - Episodes of ataxia, dysarthria and sometimes lethargy
PDH Deficiency
Clinical Features

- Spontaneous attacks

- Provoked attacks
  - Intercurrent infection
  - Stress
  - High carb meal

- Recur at irregular intervals

- May last 1 day to several weeks
PDH Deficiency
Clinical Features

- Severity of sx reflects level of enzyme activity
- Generalized weakness, areflexia, nystagmus/other ocular movement disturbances
- Ataxia is the predominant sx
- Intention tremor and dysarthria
- Hyperventilation from metabolic acidosis
PDH Deficiency
Diagnosis

- During an attack
  - Elevated lactate and pyruvate

- Between attacks
  - Lactate might be elevated
  - Pyruvate concentration is elevated
  - Lactate to pyruvate ratio is low
  - Some may have hyperalaninemia

- Dx - enzyme activity in culture fibroblasts, leukocytes or muscle
PDH Deficiency Management

- Ketogenic diet (high fat/low carbs)
- Thiamine
- Daily acetazolamide
  - May abort/prevent attacks
- Mitochondrial cocktail has not proven efficacious
Progressive Disorders
Friedrich Ataxia

- Loss of function - frataxin gene
  - Chromosome 9q13
  - Expanded GAA repeat in intron 1 of both alleles
    - 7 to 34 in normal alleles
    - 600 and 1200 triplets in most patients
    - Expansion silences gene – loss of protein
  - Ongoing somatic expansion of repeats
    - Progression of disease
  - Mitochondrial protein
    - Iron metabolism/storage
  - 1:50,000 Caucasians
Friedrich Ataxia

- Clinical criteria
  - Autosomal recessive inheritance
  - Onset before age 25
  - Ataxia of all four limbs
  - Absence of lower limb reflexes
  - Presence of pyramidal signs
    - Can present later or with preserved reflexes
Friedrich Ataxia

- Neurologically:
  - Cerebellar ataxia, often by age 5yo – progressive
    - All 4 extremities and trunk
  - Posterior column degeneration
  - Pyramidal weakness

- Cardiac:
  - Hypertrophic cardiomyopathy
    - Arrhythmia and heart failure

- Endocrine:
  - Overt DM or impaired glucose tolerance occurs
Friedrich Ataxia
Ataxia Telangiectasia

- Autosomal recessive
  - 1:20,000 to 1:100,000
    - 1.4 – 2.0% Caucasians in US heterozygotes

- Loss of function
  - Chromosome 11q22.3
  - ATM gene (for AT Mutated)
    - Expressed in all tissues in the body
    - Stalls cell cycle progression with DNA damage present to allow repair

- Heterozygotes
  - Increased risk for breast cancer
Ataxia Telangiectasia

- Clinical:
  - Progressive cerebellar ataxia (> 1yo)
  - Abnormal eye movements - various
  - Other neurologic abnormalities
    - Extrapyramidal, bulbar, motor neuron
  - Oculocutaneous telangiectasias
  - Immune deficiency
    - Poor titers to pneumococccous
    - IgG/IgA deficiency
Ataxia Telangiectasia

- Clinical cont:
  - Pulmonary disease
    - Recurrent sinopulmonary infections
    - Interstitial lung disease
  - Increased incidence of malignancy
    - 1% per year, esp leukemia/lymphoma
  - Radiation sensitivity (chemotherapy)
    - Death from low doses
  - Insulin resistance - DM
Ataxia Telangiectasia

- **Definitive diagnosis**
  - Either increased radiation-induced chromosomal breakage in cultured cells or progressive cerebellar ataxia and disabling mutations on both alleles of ATM

- **Probable diagnosis**
  - Progressive cerebellar ataxia and 3 of the following:
    - Ocular or facial telangiectasia
    - Serum IgA at least 2 SD below normal for age
    - Alpha fetoprotein at least 2 SD above normal for age
    - Increased radiation-induced chromosonal breakage

- **Possible diagnosis**
  - Progressive cerebellar ataxia and 1 of the above:
Ataxia Telangiectasia
Ataxia Telangiectasia
Questions?