Childhood Ataxia

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Definitions

- **Ataxia** is the inability to make smooth, accurate and coordinated movements.

  Ataxia can arise from disorders of:
  - Cerebellum (most common)
  - Sensory pathways (Sensory Ataxia)
    - posterior columns, dorsal root ganglia, peripheral nerves
  - Motor pathways (Paretic Ataxia)
    - Corticospinal tracts
  - Frontal lobe lesions
    - via fronto-cerebellar associative fibers

- **Cerebellar ataxia** is defined as the lack of coordination of movement that is *not* due to paresis, alternation in tone, sensory loss, or presence of involuntary movements.
Classifications:

- **Congenital**
  - Usually from CNS malformations

- **Acquired**
  - **Acute**
    - Defined as unsteadiness of walking or of fine motor movement of less than 72hrs duration in a previously well child
  
  - **Episodic and/or chronic**
    - Rare in children; usually secondary to genetic or metabolic disorder
Differential Diagnosis

**Congenital**
- CNS Malformations
  - Cerebellar hypoplasia
  - Vermian aplasia
  - Dandy-walker
  - Chiari malformation
- Joubert’s syndrome

**Hereditary**
- Autosomal recessive
  - Friedreich’s ataxia
  - Ataxia-Telangiectasia
  - Abetalipoproteinemia
  - Vitamin E deficiency
- Autosomal Dominant
  - Spinocerebellar Ataxias

**Acute/Sub-acute**
- Infectious/Immune-mediated
  - Acute Cerebellar Ataxia*
  - Acute disseminated encephalomyelitis*
  - Meningoencephalitis
  - Acute labyrinthitis
  - Multiple sclerosis
- Drug/Toxin-related*
  - Alcohol, BZDs, anticonvulsants, heavy metals, carbon monoxide
Differential Diagnosis

- **Acute/Sub-acute (cont.)**
  - Mass lesions
    - Tumor
    - Vascular lesions (AVM)
    - Abscess
  - Trauma
    - Hemorrhage
    - Post-concussion
    - Vertebral artery dissection
  - Para-neoplastic
    - Opsoclonus-myoclonus (neuroblastoma)

- Sensory ataxia
  - Guillan-Barre
  - Multiple sclerosis

- Pareitic ataxia
  - Frontal lobe lesion

- Other
  - Basilar migraine
  - Benign paroxysmal vertigo
  - Non-convulsive seizures
  - Inborn errors of metabolism
  - Hysterical gait disorder
  - Cogan syndrome
Clinical History

- Chief complaint is usually refusal to walk, “staggering” gait, or clumsiness
- Initial evaluation should focus on excluding serious causes of acute ataxia
  - R/O Mass lesions, CNS infection, hydrocephalus
- Age at disease onset, progression rate, accompanying symptoms, exposure to toxins and mode of inheritance should always be considered
Clinical History

History should include:

- Antecedent or current symptoms of infection
- Recent immunizations
- Recurrent or persistent headache, vomiting or diplopia (signs of increased intracranial pressure)
- Drug ingestion
- Recent head or neck trauma
- h/o previous similar episodes or + family history
Physical Exam

- **Mental status**
  - Helps differentiate between ACA and more serious conditions (ingestion, ADEM, +/-mass lesions)
  - Ophthalmologic exam
  - Nystagmus: common in cerebellar disorder
  - Papilledema or cranial nerve palsy: intracranial focus lesion or hydrocephalus
  - Pupillary abnormalities: mass lesion, stroke, intoxication

- **Tone/strength**
  - Asymmetry uncommon in acute cerebellar ataxia
  - Must differentiate poor coordination from weakness
  - Muscle tone usually preserved in cerebellar disorders
  - Evaluate DTRs
    - Hyperreflexia/areflexia- suggest causes other than cerebellar ataxia
Physical Exam:

Cerebellar Signs

- **Gait**- wide based gait, staggering
- **Posture**- truncal, head titubation
- **Dysarthria**- fluctuations in rhythm, tone, volume, clarity (scanning speech, slurring, dysprosody)
- **Dysmetria**- poor coordination of voluntary movements
  - finger-to-nose (upper extremity) or heal-to-shin (lower extremity), dysdiadochokinesia, intention or kinetic tremor
- **Oculomotor**- gaze-evoked nystagmus, impairment of smooth pursuit

Findings remain unchanged with eyes open or shut with cerebellar ataxia! (i.e. negative romberg)
Localization of Cerebellar Lesions

- **Vermal (midline) lesions:**
  - Truncal and gait abnormalities, oculomotor disturbances
  - Speech is spared

- **Hemispheric lesions:**
  - Ipsilateral limb hypotonia, dysmetria, and tremor
    - Patients veer to the affected side when walking
  - Dysarthria

- **Deep cerebellar nuclei**
  - Resting tremor, myoclonus, opsoclonus
Evaluation of the Ataxic Child

- Primary aim of laboratory and radiologic investigations is to identify serious conditions mimicking post-viral ataxia
  - Post-viral (ACA) is a diagnosis of exclusion

- **Urine and/or serum toxin screen**
  - Recommended in all children with acute or episodic ataxia

- **Neuroimaging with CT or MRI**
  - Recommended in all children with acute or sub-acute onset of ataxia (controversial)
  - Others recommend imaging only with atypical presentation or no spontaneous improvement after 1-2 weeks
  - low yield in the absence of altered MS, focal neurologic findings

- **CSF examination**
  - Indicated when inflammatory or infectious disorders are suspected
  - Pleocytosis and elevated protein can be seen in ACA
Evaluation of the Ataxic Child

- Further diagnostic testing should be guided by considering the mode of inheritance, age at disease onset, progression rate, and accompanying symptoms

- **Electrophysiology testing**
  - Nerve-conduction studies - peripheral neuropathies
  - VEP, SEP, AEPs - demyelinating disease

- **Genetic testing**
  - Friedreich’s ataxia, Ataxia-Telangiectasia, SCAs

- **Metabolic work-up**
  - Pyruvate, lactate, ketones, LFTs, urine organic and serum amino acids (inborn error of metabolism)
  - Urinary catecholamines, abdominal imaging (neuroblastoma)
  - Vitamin E, lipids (abetalipoproteinemia)
  - Alpha-feto protein (ataxia-telangiectasia)
Acute Cerebellar Ataxia

- Most common cause of childhood ataxia accounting for 40% of all cases
- Most common in children 2-4 yrs (almost always <6 yrs)
- Onset is sudden with predominant symptom of truncal ataxia, uncoordinated gate, mental status is normal
- “pure” acute cerebellar ataxia is not associated with fever, seizures, or other systemic signs (consider acute disseminated encephalomyelitis)
Acute Cerebellar Ataxia

- Post-infectious cerebellar demyelination
  - Autoimmune phenomenon incited by infection w/ cross-reaction of Abs against cerebellar epitopes
  - History of antecedent illness 5-21 days prior to onset is obtained in ~70% of patients
  - ~1/4 of cases are preceded by Varicella infection, but numerous agents have been implicated (EBV, Coxsackievirus, Echovirus, Enterovirus)
  - Vaccinations have been implicated (esp measles) but causal relationship has not been proven
Acute Cerebellar Ataxia

- Neuroimaging is usually normal
  - rare cases demonstrate focal cerebellar lesions on MRI
- Diagnosis of exclusion
- Supportive treatment (although steroids and IVIG have been beneficial in select cases)
- Ataxia improves in a few weeks but may last up to 2 months
- Prognosis for complete recovery is excellent (>90%); however, a small number have long-term sequelae
Acute Disseminated Encephalomyelitis

- Multi-focal immune-mediated demyelinating disease following a viral illness
- Mean age 6-8 years old
- Distinguished from ACA by alteration of mental status and/or presence of focal neurological deficits (seizures, hemiparesis, cranial neuropathies) and systemic symptoms
- MRI reveals multi-focal demyelinating lesions in white/gray matter, cerebellum
  - MRI findings are similar to those seen in multiple sclerosis
- Treatment: steroids or IVIG
- Prognosis: recovery occurs over 4-6 weeks; 60-80% have normal neurological outcomes
Toxic Cerebellar Syndromes

- Drug ingestion accounts for ~1/3 of all cases of acute ataxia in children
- Anticonvulsants (dilantin, tegretol), lithium, BZDs, alcohol and antihistamines are common offenders (also heavy metals, solvents)
- Bimodal age distribution
  - Young children < 6 with accidental ingestions
  - Adolescents as a result of substance abuse
- Mental status changes w/ lethargy, confusion, inappropriate speech are common
- Diagnosed via urinary and/or serum toxin screen
Mass Lesions

- 45-60% of all childhood brain tumors arise in the brain stem or cerebellum.
- Posterior fossa tumors usually present with slowly progressive ataxia and symptoms of increased ICP.
- Focal neurologic findings are common (papilledema, cranial nerve palsies, hemiparesis).
- Common infra-tentorial tumors:
  - Astrocytomas: account for >50% of all primary CNS malignancies; most common brain tumor of childhood.
  - Medulloblastoma: arises from the cerebellum; most common malignant brain tumor in children; 40% of all posterior fossa tumors.
- MRI allows better visualization of cerebellum and is the recommended study (lack of bone artifact, high resolution and capability of imaging different planes).
Patient’s MRI
Ataxia-Telangiectasia

- Autosomal recessive
- Most common degenerative ataxia
- Age of ataxia onset is ~15mo-2yrs with progression to loss of ambulation by adolescence
- Clinical manifestations include progressive ataxia, oculomotor dysfunction, oculocutaneous telangiectasias (present around age 5)
- Combined B and T cell immunodeficiency (decreased IgA, IgG2, CD4 T cells); presents with recurrent sinopulmonary infections
- Increased risk of malignancy (lymphoma, leukemia, HD, brain tumors)
- Laboratory investigation reveals increased alpha-fetoprotein and decreased immunoglobulins, CD4 cells
Telangiectasias

Telangiectasia presents *after* the diagnosis should already have been confirmed by the presence of ataxia and infections.
Friedreich’s Ataxia

- Autosomal recessive
- Age of onset between 10-15 years (before 25)
- Mutation in gene encoding a mitochondrial protein *fraxatin* which leads to iron overload and increased production of free radicals
- Clinical features: progressive *sensory* ataxia, impaired vibration and position sense, areflexia of lower extremities, progressive weakness of LEs, oculomotor disturbances, dysarthria, hearing impairment, reduced visual acuity
- Non-neurologic features: skeletal deformities (scoliosis), hypertrophic cardiomyopathy, diabetes mellitus
- Cognition is normal
- Prognosis: wheel-chair bound by 10-12 yrs. Median survival after disease onset is ~35yrs