Acute Ataxia in Children

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Practice Gaps

The word *ataxia* in medicine frequently is used to signify not only difficulty walking but also difficulty walking specifically due to cerebellar dysfunction. However, although gait and cerebellar disorders can overlap, they are not synonymous. The purpose of this review is to illustrate how children with difficulty walking present, which includes, but is not limited to, patients with cerebellar disorders. In addition, the goal is to illustrate both the more common and the more urgent causes of acute ataxia in children.

Objectives After completing this article, readers should be able to:

1. Recognize the most common and the most urgent causes of acute ataxia in children.
2. Recognize that ataxia is a nonlocalizing complaint, frequently misinterpreted as being localized entirely to the cerebellum.
3. Take the first steps in the evaluation and management of acute ataxia.

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ABBREVIATIONS

ACA	acute cerebellar ataxia
ADEM	acute disseminated encephalomyelitis
CSF	cerebrospinal fluid
CT	computed tomographic
GBS	Guillain-Barre syndrome
ICH	intracerebral hemorrhage
ICP	intracranial pressure
IV	intravenous
IVIg	intravenous immunoglobulin
MRI	magnetic resonance imaging
NMDA	*N*-methyl-D-aspartate
OMS	opsoclonus-myoclonus syndrome
TM	transverse myelitis
tPA	tissue plasminogen activator
WBC	white blood cell

Acute ataxia is fairly common in children. The most common cause, acute cerebellar ataxia (ACA), is estimated to occur in 1 in 100,000 children. (5) The causes of acute ataxia in children are typically benign but at times can represent serious illness. The comprehensive range of potential causes is broad, but typical causes are few and have changed in the post–varicella vaccine era. Ataxia is also frequently thought to represent cerebellar disease but can, in fact, be due to dysfunction of any part of the nervous system or occasionally nonneurologic mechanisms. This paper reviews the common causes of acute ataxia in children, as well as less common causes that should not be missed. It attempts to aid the reader in approaching the neurologic examination, as well as the first steps in the management of the ataxic child.

Ataxia derives from the Greek—*a* (without), *taktos* (order)—and means a lack of order. Broadly, ataxia encompasses disorders in which there is an absence of coordinated motor movements, often involving gait; however, gait disorders can also present with dysfunction not due to cerebellar dysfunction. Both can rightly be called ataxia. In other words, ataxia is a nonlocalizing complaint. It can emerge from disorders affecting the brain through the spinal cord, as well as peripherally from nerves to muscles. Attempting to localize the

source of dysfunction should guide the history, examination, and subsequent studies. As such, the history and examination should be directed at determining whether the patient has a disorder of coordinated movements, ie, cerebellar dysfunction, or is struggling to walk due to other causes.

Although ataxia can certainly be chronic, subacute, or intermittent, it is usually acute as a presenting symptom in children. This review focuses primarily on acute ataxia, typically defined as ataxia for less than 72 hours, with particular attention to specific diagnoses and relevant diagnostic testing. For the treating physician, the list of its potential causes can be daunting, (1) in part because ataxia can by caused by dysfunction at any level of the motor system, from brain to muscle (Table 1). It can even be due to sensory impairment. Diagnostically, the goal is to localize the ataxia to the level of dysfunction. Practically, the initial approach to the child with acute ataxia should focus on the serious causes of ataxia. Once these have been excluded clinically, more common as well as treatable causes can be considered. Life-threatening conditions fall into 4 broad categories: infection and/or inflammation, neoplasm, stroke, and ingestion. This review discusses the initial steps when approaching the patient with acute ataxia, followed by a limited discussion of management.

HISTORY

Although the initial history should be directed foremost at identifying serious causes of acute ataxia, in most patients the causes of acute ataxia are self-limited and benign. One retrospective study of 40 pediatric cases found that 80% could be attributed to ACA, toxic ingestion, and Guillain-Barre syndrome (GBS). (6) The history should explore evidence of recent or current infection: fever, rash, respiratory symptoms, or vomiting. Questions about possible toxic exposures in the home, such as medications, alcohol, or illicit drugs, are essential. The possibility of trauma, observed or potentially unobserved, should be explored with all caregivers and children who might be aware of it.

Associated symptoms can further guide the history. For example, although ACA is characterized by preservation of alertness, a change in mental status is concerning and can signal a systemic process, brain tumor, or cerebellitis. Headaches, recurrent vomiting, vision loss or diplopia, and worsening of symptoms when supine can be signs of elevated intracranial pressure (ICP) from hydrocephalus in the setting of posterior fossa masses. Note, however, that these findings can be late or even intermittent, and their absence does not exclude elevated ICP from any cause. Considerations involving ataxia with altered mental status include toxic ingestion, infection, or mechanical compression of the brain stem by a tumor or abscess. Recent and abrupt onset of symptoms is more suggestive of a vascular, toxic, or infectious cause. Tumors and immune-mediated processes are typically more subacute in their progression. Previous similar episodes are suggestive of chronic conditions such as migraine, vestibular dysfunction, or even seizures. Recurrent episodes are also potentially suggestive of metabolic processes (Table 1).

Life-threatening causes of acute ataxia typically originate in the central nervous system. Altered mental status, vomiting, or visual disturbances in the presence of ataxia are red flags. Life-threatening causes typically involve the posterior fossa and/or brain stem. In particular, symptoms refer to 3 sources: the cranial nerves, the pyramidal tracts, and the cerebellum. Moreover, the involvement of brainstem and cerebellar structures typically results in abnormalities on both history and physical examination. As such, a normal neurologic examination, carefully performed, is a pertinent negative.

PHYSICAL EXAMINATION

The physical examination begins with vital signs. Fever suggests infection. Hypertension is nonspecific but can be caused by elevated ICP, eg, in ischemic or hemorrhagic stroke or acute hydrocephalus. Elevated BP and/or tachycardia can also occur with peripheral processes such as GBS.

GENERAL EXAMINATION

Initial observations (eg, Does the child appear ill or uncomfortable? Is he or she agitated or taking care not to move?) are valuable. The examination can be challenging because the child may be uncooperative. Given this, the examination should move from the least to the most invasive.

The somatic examination should explore for evidence of meningismus: neck stiffness with flexion and photophobia and discomfort with extraocular movement. On occasion, acute ataxia or vertiginous gait may be caused by acute otitis media. Otitis media, tender red mastoid, or mastoid bruits suggest infectious mechanisms, vestibular disorders, or venous occlusive disorders. Any process causing lower extremity or back pain may produce a gait disturbance termed *antalgic gait*. Careful inspection of toes, nails, foot structure, and all lower extremity joints, in addition to back spasm, scoliosis, and spinal deformities, may reveal that the cause of gait dysfunction is from antalgic gait even without the complaint of pain, particularly in younger children.

TABLE 1. **Selected Causes of Acute Ataxia in Childhood**

INFECTIOUS OR PARAINFECTIOUS	VASCULAR	GENETIC/METABOLIC
Acute cerebellar ataxia	Arteriovenous malformation	Abetalipoproteinemia
Acute cerebellitis	Vasculitis	Arginosuccinic aciduria
Opsoclonus-myoclonus ataxia	Ischemic stroke	Vitamin E deficiency
Transverse myelitis	Intracerebral hemorrhage	GM2 gangliosidosis
Guillain-Barre syndrome		Hartnup disease
Coxsackievirus	**TOXIC**	Hyperalaninemia
Echovirus	Alcohol	Hyperammonemia
Epstein-Barr virus	Lead encephalopathy	Hypoglycemia
Mumps encephalitis	Benzodiazepines	Kearns-Sayre syndrome
Japanese B encephalitis	Opioids	Leigh disease
Mycoplasma pneumoniae	Antihistamines	Maple syrup urine disease
Pertussis		Myoclonic epilepsy with ragged red fibers
Polio		Metachromatic leukodystrophy
Enterovirus D68	**TRAUMATIC**	Adrenoleukodystrophy
Tuberculosis	Acute cerebellar edema	Mitochondrial complex defects
Varicella virus		Biotinidase deficiency
Borrelia burgdorferi	**PSYCHOGENIC**	Neuronal ceroid lipofuscinosis
Powassan virus	Conversion reaction/functional	Sialidosis
NEOPLASTIC		Niemann-Pick disease
Cerebellar or frontal tumors	**MISCELLANEOUS**	Refsum disease
Neuroblastoma	Hydrocephalus/shunt dysfunction	Neuropathy, ataxia, retinitis pigmentosa
Pontine tumors	Complex migraine	Wernicke encephalopathy
Spinal cord tumors		Tryptophanuria
		Triosephosphate isomerase deficiency

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Pupil abnormalities suggest many etiologies, such as toxins and drugs (large from atropinergic agents or small from opiates) or third nerve compression resulting in ptosis, enlarged pupil, and ocular abduction. Torticollis, head tilt, or any resistance to neck motion suggests a craniocervical junction disorder such as Chiari malformation, cervical cord compression, or posterior fossa tumors. Impairment of extraocular movement from a pontine glioma, medulloblastoma, or cerebellar astrocytoma may cause a head tilt without restriction of head/neck range of motion. Acute gait disorders may be nonneurologic and caused by psychogenic mechanisms. The analysis of nonneurologic gait disorders is complex and is discussed separately in this review.

NEUROLOGIC EXAMINATION

Neurologic evaluation begins with the child's mental status. Behavioral changes, decreased alertness, inattention, or dysarthria can all be clues to elevated ICP, brainstem compression, or cranial neuropathies that may affect eye movements. Fundi should be inspected for papilledema. Evaluating for disc blurring can be difficult; sometimes the presence or absence of venous pulsations is more evident. The absence of venous pulsations can be due to elevated ICP. The presence or absence of further associated findings to suggest elevated ICP, such as restriction of upward gaze or lateral eye movements, should also be noted.

Initially it is ideal to observe a child's gait in a natural setting, such as while walking into the examination room or

office. To reduce artificial or unnatural gait patterns induced by intense observation or merely the request to walk, it is useful to throw a ball and ask the patient to both walk then run to pick up the ball. Ataxia and other gait disturbances may be best revealed as the patient turns to walk back. Patients with narrow-based gait are unlikely to have cerebellar pathway diseases.

Cerebellar hemisphere dysfunction is often associated with a wide-based gait. Forms of identifiable cerebellar dysfunction discernible on examination are manifold. Cerebellar ataxia includes abasia (unsteady stance), dysmetria (impaired excursions in movement), dysdiadochokinesis (nonrhythmic and impaired alternating movements), dyssynergia (decomposition of movement into sequential tasks), or truncal ataxia if the cerebellar vermis is involved.

However, ataxia—understood as a gait disorder—can also refer to the cranial nerves or motor or sensory impairments. In cooperative patients one should first evaluate for dysmetria in each upper extremity. If the index finger misses the target it may be from cerebellar dysfunction, weakness, or impaired vision. To distinguish among these, one should first look for dysdiadochokinesis—a cerebellar finding. Alternatively, diplopia can cause patients to miss the target. Covering 1 eye of the patient typically eliminates diplopia. In patients with diplopia, each eye and its movements should be evaluated individually. The presence of ptosis is most commonly due to Horner syndrome or third nerve palsy. To identify limb weakness, one should have the patient extend both arms out horizontal to the floor "as if holding a pizza tray." The presence of drift, ie, gradual lowering of one arm, suggests ipsilateral arm weakness, and a full motor examination is necessary. Unilateral weakness or pyramidal tract dysfunction manifests as asymmetries in arm or leg use. Subtle gait difficulties can be elicited with tandem walking or running; impaired arm swing suggests ipsilateral weakness

A lurching gait or falling to one side is typical with vestibular dysfunction (often confused for cerebellar dysfunction in young children who cannot describe the subjective experience of vertigo). Sudden lurching or falling to one side triggered by head rotation suggests vestibular dysfunction.

Sensory ataxia also causes a positive Romberg test, which examines the dorsal columns. Attempts to stand with feet close together can result in swaying from side to side with eyes open or closed (termed a positive Romberg test when the eyes are closed). A positive test is one in which swaying or a frank fall occurs. Young children with acute lower extremity weakness from GBS or myositis may manifest ataxia and falling, a gait disturbance termed *pseudo-ataxia*. Muscle stretch reflexes can provide essential information but can also mislead the examiner. Evaluation for presence or absence is particularly important when there is suspicion for GBS. More generally, however, asymmetrical reflexes and the presence or absence of upgoing toes (the latter an upper motor neuron sign) can be misleading. These findings should be interpreted cautiously and used as supportive evidence of suspected underlying central or peripheral processes, prompting further evidence of motor or sensory impairments. For example, asymmetrical brisk reflexes alone may be pathologic or may be an artifact of patient positioning, and exaggerated reflexes with ipsilateral atrophy and weakness suggest chronic corticospinal involvement.

DIFFERENTIAL DIAGNOSIS

There are 2 intersecting axes to draw from the history and examination: localization of the disorder and pathology. When first evaluating a patient, the tempo of presentation can provide clues to pathology. For example, infection and immune-mediated disorders are typically acute to subacute and frequently affect multiple systems. Ischemic strokes typically present with maximal deficit and an acute onset, whereas complex migraines evolve over 15 to 30 minutes. Brain tumors are chronic but can present acutely in the presence of acute hemorrhage, cerebrospinal fluid (CSF) obstruction, or seizure.

The potential causes are listed in the following subsections in an order attempting to synthesize a combination of both most urgent and most likely diagnoses. Strokes are uncommon but urgent; migraines are common but not urgent. Immune-mediated processes are very common and potentially urgent. Table 2 lists the relative frequency of etiologies for acute ataxia.

Vascular

Stroke is the most urgent, if not the most likely, consideration. Hemorrhagic stroke, ie, acute intracerebral hemorrhage (ICH), is a neurologic emergency. Large hemorrhages causing mass effect or cerebellar hemorrhages threatening the brain stem require urgent neurosurgical evaluation and treatment. The most common cause of spontaneous ICH in children is arteriovenous malformation. (2) A noncontrast head computed tomographic (CT) scan is the best initial diagnostic test for ICH, performed urgently.

Ischemic strokes can also cause ataxia. Ideal imaging (CT vs magnetic resonance imaging [MRI]) should be discussed urgently with a neurology consult based on time of presentation and degree of clinical suspicion for stroke. With all ischemic strokes, the first question to ask is, "Can tissue plasminogen activator (tPA) be given?" tPA is a thrombolytic

therapy for ischemic stroke. It can be given systemically intravenously (IV) for ischemic strokes in patients seen less than 4.5 hours after onset. After this time, efficacy decreases and there is higher risk of cerebral hemorrhage. tPA can also be given intra-arterially by interventional neuroradiologists. Intra-arterial tPA can be given up to 6 hours after onset. tPA is most commonly given for adults but is used increasingly in pediatric patients. (3)

The level of evidence in children for tPA is limited to expert opinion. Its use is off-label in children and limited to certain pediatric stroke centers; however, if the clinical presentation is suggestive of an ischemic stroke, urgent transfer to a pediatric stroke center should be considered.

Trauma

Life-threatening conditions to consider in the setting of trauma are hemorrhagic stroke resulting in contusion(s) and ischemic stroke from arterial dissection. In the absence of more diffuse axonal injury causing associated encephalopathy, it is unusual for trauma to present with isolated ataxia. The important exception to this rule is arterial dissection, which represents 5% to 25% of pediatric ischemic strokes. The vertebral arteries supply the posterior circulation and cerebellum. Presenting signs and symptoms refer to the posterior fossa: ataxia, vertigo, vomiting, diplopia, and head and neck pain. Although these symptoms are common and nonspecific, 88% of patients in a recent review had focal neurologic deficits. (3) Fifty percent of children in the same study had a history of trauma. Cerebral concussion may cause vertigo, gait disturbance, and a positive Romberg test, often termed *vestibular concussion,* and it is frequently underdiagnosed in our experience.

Toxic Ingestion

Ingestion of a toxin represents a major cause of ataxia in children, accounting for approximately 10% (7) and up to one-third (4) of cases. Sending a urine sample to toxicology, particularly in children younger than 5 years, is a high-yield and efficient practice. In our experience, the most common presentation of toxin ingestion is a combination of ataxia and somnolence without antecedent illness. In addition, there can be a discrepancy between the high degree of unresponsiveness and patients' otherwise overall benign appearance. After ingestion, patients can simply appear to be sleeping. Vital signs are often normal. Although urine toxicology screens do not identify many prescription medications, they do identify the most urgent: benzodiazepines and opioids, which can impair respiration. Accidental ingestion occurs in young children. Adolescents can also present after ingestion in attempts to self-harm. Symptoms of ingestion can be nonspecific. Indeed, when symptoms do not fit well into a clinical syndrome, and

TABLE 2. **Acute Ataxia Etiologies**

ETIOLOGY	PATIENTS, NO. (%) (N = 120)
Postinfectious cerebellar ataxia	71(59.2)
Drug intoxication	10 (8.3)
Opsoclonus-myoclonus ataxia	10 (8.3)
Acute cerebellitis	3 (2.5)
Cerebellar stroke	2 (1.7)
Acute disseminated encephalomyelitis	2 (1.7)
Meningitis	1 (0.8)
Cerebral vein thrombosis	1 (0.8)
Miller Fisher syndrome	1 (0.8)
Concussion	1 (0.8)
Genetic (first episode of episodic ataxia (n = 5), Leigh syndrome (n = 1), undiagnosed (n = 1)	7 (5.8)
Idiopathic	11 (9.2)

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when these symptoms spontaneously improve within 12 to 24 hours, ingestion should become a concern. A thorough history of medications in the home(s) or child care is essential. When considering toxic ingestion, it is also important to evaluate for other evidence of metabolic aberrations, such as hypoglycemia, hyponatremia, and hyperammonemia.

Immune-Mediated/Postinfectious Causes

ACA, Cerebellitis, Opsoclonus-Myoclonus Syndrome. ACA is the most common cause of acute ataxia in children. It is a benign, typically postinfectious or parainfectious phenomenon. Presentation is fairly characteristic, but it needs to be distinguished from more worrisome causes of ataxia that can initially look similar, namely, opsoclonus-myoclonus syndrome (OMS) or cerebellitis.

ACA typically occurs in preschool- and school-aged children. Generally, the acute ataxia is most prominent on awakening and improves over the course of days to weeks or, rarely, months. Nystagmus is uncommon. Truncal ataxia with trouble sitting and appendicular intention tremor are typical findings. Children are afebrile, alert, and well-appearing.

Acute cerebellitis is likely the extreme end of a continuous clinical phenomenon, with ACA representing the milder end. Clinically, patients with cerebellitis appear more ill than those with ACA. Patients with cerebellitis have ataxia as well as further symptoms, such as vomiting, altered mental status, increased sedation, or seizures and abnormal brain imaging findings. Numerous case reports of fulminant presentations with varying outcomes have been reported. (5) Initial presentation can be fulminant or subacute. Unlike its more benign form, fulminant cerebellitis progresses from its onset to the development of encephalopathy, with hydrocephalus caused by obstruction of the fourth ventricle. Unlike ACA, outcomes of cerebellitis are not always favorable but can potentially be improved with aggressive management: typically, CSF diversion and/or corticosteroids with supportive ICU care.

Connolly et al (6) described a cohort of 73 patients with ACA in 1994. This study predates wide adoption of the varicella vaccine. In 78% of these patients, a preceding viral illness was identified (19 patients with varicella and 2 with Epstein-Barr virus). Two cases were associated with vaccines, and the rest were idiopathic. The latency of known precipitant to onset was 1 to 43 days. On follow-up, at least 90% of patients had made a full recovery.

A more recent cohort (Table 2) of pediatric patients presenting with ataxia was published in 2016. (7) This was a retrospective review of all patients (N = 120) presenting with ataxia to Children's Hospital of Pittsburgh from 2003 through 2013. Of patients with acute ataxia, 82% were 1 to 6 years old and 16% were 6 years or older, with an overall age range of 6 months to 18 years.

Of this cohort, 71 patients (59%) had ACA; 85% of patients with ACA were 1 to 6 years old, 15% were older than 6 years, and none were younger than 1 year. Mean time to presentation was 8.2 days. In this post–varicella vaccine era study, none of the patients had varicella. Only 2 cases were attributed to vaccines. Of the 71 patients, 58 had a lumbar puncture, of whom 40% had a CSF pleocytosis (range, 6–60 cells/mm^3). In addition, many patients were tested for varicella, Epstein-Barr virus, herpes simplex virus, cytomegalovirus, and enterovirus by CSF polymerase chain reaction; all were negative. Finally, brain MRI was performed in 69 of 71 patients, and all the results were normal.

In follow-up, 91% of patients had recovered by 30 days, the remainder by 6 months. Three patients received intravenous immunoglobulin (IVIg), with recovery at 2 to 4 months. Three patients received corticosteroids, with recovery at 2 to 4 weeks. Indications for immune-modulating therapy were not discussed.

Cerebellitis was found in 3 of the 120 patients. All 3 patients had concurrent viral respiratory infections; 1 required decompressive craniotomy. These patients were aged 16 months to 8 years. Vomiting and headache were present in the 6- and 8-year-olds. All the patients "appeared ill," had an elevated white blood cell (WBC) count or protein level in the CSF, and had abnormal findings on brain MRI, with signal hyperintensities in the cerebellum. One patient had recovered at 3-month follow-up, the 16-month-old had cognitive difficulties and ataxia at 3-month follow-up, and the third patient was lost to follow-up.

Of considerable interest is that in this cohort the number of patients presenting with ataxia due to OMS was the same as ingestion. Although this likely represents referral patterns to a large academic center, it also suggests that OMS may be more frequent than generally recognized, and this mirrors the authors' experience.

OMS is an immune-mediated, paraneoplastic encephalopathy seen most commonly in children younger than 4 years. (8) It has also been described as opsoclonus-myoclonus ataxia. Indeed, on initial presentation it may not be distinguishable from ACA. However, unlike ACA, patients with OMS both do not show rapid improvement and either present with or develop additional features, including developmental regression, feeding difficulties, irritability, sleep disturbance, and paroxysmal movements. Opsoclonus describes intrusive, rapid, saccadic eye movements. In the authors' experience, opsoclonus can be a late

finding and, along with myoclonus, can be extremely brief and intermittent. Nevertheless, if a patient with suspected ACA is not improving as expected, is encephalopathic, or has paroxysmal limb or eye movements, it is essential to consider OMS. Once the diagnosis is made, the patient requires evaluation for occult neuroblastoma or ganglioneuroblastoma associated with OMS. Even when not identified, the presumption is that a small tumor with regression may have been present. Retrospective observational evidence suggests that aggressive immune therapy with a variety of agents, including but not limited to corticotropin, IVIg, and rituximab, has positive effects on the disordered immune response. (9)

Acute disseminated encephalomyelitis (ADEM) is an acute demyelinating event that is typically most severe at onset. It is an immune-mediated encephalitis with or without myelitis often occurring in the context of viral or postviral infections. The white matter of the brain and spinal cord are preferentially affected. Typically, ADEM follows a prodrome of fever, vomiting, headache, and malaise. The neurologic features are broad: unilateral or bilateral pyramidal signs (60%–95%), acute hemiplegia (76%), ataxia (18%–65%), cranial nerve palsies (22%–45%), visual loss from optic neuritis (7%–23%), seizures (13%–35%), and spinal cord involvement (24%). (10) Current therapy, based on limited case reports and observational studies, is typically methylprednisolone, 10 to 30 mg/kg IV daily (maximum of 1 g daily), followed by a 4- to 6-week corticosteroid taper. (11) IVIg and plasmapheresis have also been used in refractory or recurrent cases. (12)(13) Although outcomes are typically good, there is emerging evidence of long-term effects, such as impaired brain growth (14) as well as subtle neurocognitive impairments in selected patients. (15)

Finally, more recent case series have identified novel causes for immune-mediated ataxia in childhood. Anti–*N*-methyl-D-aspartate (NMDA) receptor encephalitis is a common, autoimmune cause of encephalitis in children. NMDA receptor encephalitis was the most commonly identified cause of pediatric encephalitis in the California encephalitis project. (28) It was greater than 4 times more common than identified viral etiologies. NMDA receptor encephalitis has been identified in young patients (age <4 years) presenting with ataxia, followed by the more typical disturbances of sleep, autonomic dysfunction, encephalopathy, and sometimes seizures. (16) Paraneoplastic cerebellar degeneration due to voltage-gated P/Q-type calcium channel antibodies has also been described. (17)

Transverse Myelitis. Children with transverse myelitis (TM) may present with acute back pain associated with sensory or motor symptoms. (18) Urinary retention is common. Burning limb pain or sensory loss may be reported. Limb weakness is typical. Muscle stretch reflexes may be exaggerated or diminished. If the latter, distinguishing acute TM from GBS may be challenging. However, the presence of a sensory level and urinary retention are more suggestive of TM.

TM is an acute neurologic emergency. Urgent evaluation with MRI of the spine is required for TM and other potential myelopathic disorders, such as arteriovenous malformation with hemorrhage, epidural hematoma, or spinal cord tumor.

When TM is suspected, empirical treatment with corticosteroids should be considered. There is no clear evidence that corticosteroids worsen mimics of TM, such as spinal strokes, infections, or tumors. Retrospective data suggest improved outcomes in patients receiving corticosteroids early. (19) Therefore, a dose of methylprednisolone, 30 mg/kg per dose (maximum of 1,000 mg) IV, even as evaluation with imaging and lumbar puncture is underway, likely has rewards that outweigh the risks.

Labyrinthitis. The clinical symptoms of labyrinthitis are superficially similar to those of ACA: acute onset of ataxia, vertigo, and nystagmus. However, children with acute labyrinthitis generally appear more ill, have prominent vomiting, and hold themselves still to minimize exacerbation of symptoms. Nystagmus is the exception in ACA; it is typical with labyrinthitis. Movement worsens the vertigo. This condition frequently occurs in clusters of exposed individuals, most frequently in spring and early summer, supporting an infectious (likely viral) cause. In particular, the vestibular nerve is inflamed. In our experience, ACA is far more common in children younger than 5 years, and labyrinthitis is more common in children older than 5 years. A 2004 study of vestibular neuritis in adults found that vestibular function was improved in patients treated with methylprednisolone but not with valacyclovir. (20)

Guillain-Barre Syndrome. Studies of the incidence of GBS in children younger than 16 years, most of which have been performed in Europe and North America, suggest rates between 0.4 and 1.4 per 100,000. (21) Although the typical presentation of symmetrical weakness is well-known, an acute progressive ataxia is another presentation of GBS seen particularly in young children. Important early clues include distal paresthesia or numbness. Leg pain is not uncommon. Younger children may present with prominent symptoms of leg pain, agitation, or vomiting, and meningeal signs may be present on examination. Muscle stretch reflexes are depressed or absent but can be present on initial presentation. Lumbar puncture typically demonstrates dissociation between cells and protein, with elevated protein and

borderline-to-normal WBC counts. The CSF may be normal on initial presentation. Three additional types of disorders need to be considered in the setting of suspected GBS. First, TM can also present with limb weakness, back pain, and depressed reflexes. Sustained urinary or bowel sphincter dysfunction and a sensory level distinguish TM from GBS. Second, tick paralysis can also present with pure motor weakness and absent reflexes. Particularly in the late spring or summer, if careful inspection reveals a tick, its removal is typically curative. Third, oculomotor paralysis can be a clue and can appear similar to the Miller Fisher variant of GBS, characterized by ataxia, oculomotor palsies, and absent deep tendon reflexes. Finally, brainstem encephalitis can also mimic the Miller Fisher variant of GBS.

Treatment is typically with IVIg, 0.4 g/kg IV daily for 5 days. A multicenter trial of 95 children suggested that treatment hastens recovery and decreases relapse but does not clearly affect overall outcome. (22)

Myasthenia Gravis. Myasthenia gravis presents with fluctuating pure motor weakness. Children may present with recent inability to walk that has since resolved but has been occurring repeatedly. Frequently there is evidence of concomitant ptosis or pharyngeal weakness. The fluctuating weakness can lead to falsely attributing weakness to a psychogenic cause. Therefore, examination should be directed toward evidence of fatigable weakness. Infectious illness can exacerbate myasthenic patients, causing them to present with acute weakness. Diagnosis is typically made using repetitive stimulation on electromyography/nerve conduction studies and with corroborating serum antibodies to synaptic antigens.

Infectious. During the prevaccine era, varicella was classically associated with ACA. In the post–varicella vaccine era, this is no longer the case. (23) However, beginning in 2014, enterovirus D68 emerged with a spike in incidence in children presenting with acute flaccid myelitis. In general, enterovirus D68 typically presents with respiratory or gastrointestinal illness in children and is most common in late summer to early fall. According to 1 retrospective review, approximately 20% of patients with acute flaccid myelitis require ICU care. (24) Acute flaccid myelitis most commonly occurs in children younger than 14 years, with a median age of 7 years, but it has been diagnosed in adults. (25) It follows the infectious prodrome and is characterized by flaccid paralysis involving 1 to 4 limbs. Weakness is commonly asymmetrical. Cranial neuropathies, particularly facial palsies, are common. Weakness develops over hours to days. Ataxia may not be the presenting complaint because upper limbs seem to be preferentially affected.

Pathologically, anterior horn cells and cranial nuclei are affected. MRI typically demonstrates longitudinally extensive, nonenhancing T2 signal change in the spinal cord. CSF typically demonstrates a mild pleocytosis (WBC count, $<100/\mu L$ [$<0.10\times10^9/L$]) and mild elevation in protein level. Virus can be identified from CSF, sputum, or stool. Empirical therapy with IVIg and/or corticosteroids has been ineffective in small cohort studies. (26)

Neoplastic

Childhood brain tumors occur most frequently in the posterior fossa. The most common tumors are medulloblastoma, brainstem glioma, ependymoma, and cystic astrocytoma. There are 3 potential areas of involvement: cranial nerves, pyramidal tracts, and the cerebellum. Although ataxia can be the presenting complaint, in the absence of hemorrhage or acute CSF obstruction it is unusual for the ataxia to be acute (new during the past 72 hours). Although symptoms may be reported to have developed over the course of days, a careful history typically reveals subtle signs of weakness and coordination difficulties lasting weeks to months. Signs from obstruction of CSF flow are common, and children younger than 2 years typically present with increasing head circumference. In older children, symptoms such as headaches and ataxia are more common. The average time from symptom onset to diagnosis is 7 months. Although less common than brain tumors, spinal tumors can also present with ataxia. Depending on the spinal level, signs of weakness or sensory loss referable to the lower or upper extremities with preservation of reflexes will be present. In addition, as noted previously herein, paraneoplastic presentation of tumors (eg, OMS) at times need to be considered in the differential diagnosis of ataxia.

Miscellaneous Causes

Migraine. Vertigo as the primary or sole manifestation of migraine occurs in 2 settings: with very young children and teenaged girls. Children younger than 4 years can have the abrupt onset of unsteadiness lasting seconds to minutes. More commonly, adolescents describe repeated bouts of isolated vertigo, or headache and vertigo. In both cases, there is usually a family history of migraine and a propensity to motion sickness in the context of a normal neurologic examination.

Psychogenic Conversion Disorder. Another challenge of clinical diagnosis includes a variety of psychogenic conversional mechanisms that impair natural gait. These conversion reactions range from unsteady gait, tripping, falling over, lurching side to side, and advancing to a very disorderly gait of weaving and bobbing called *astasia-abasia*. One meaningful clinical clue to conversional gait patterns is

derived from knowledge of physics: periodically standing on one foot while lurching side to side often excludes a primary neurologic cause because neurologically mediated impaired balance leads a patient to widen and lower the stance to lower one's center of gravity. An experienced and patient clinician is required both to work through this difficult differential diagnosis and to communicate with gentle confidence the diagnostic conclusion. For successful management of psychogenic gait disorders, it is essential that parent and physician have a shared confidence in the diagnosis. This facilitates the understanding that is required to comfortably develop and implement the patient- and family-centered intervention based on the use of limited negative laboratory studies and clinical trust.

Metabolic Disease. In the authors' experience, metabolic disease is a very uncommon presentation of acute ataxia. In the era of newborn screening, those disorders, which will present acutely, most commonly do so by age 2 years. A broad range of rare disorders will present later and more insidiously. Nevertheless, particularly in young children, sending an ammonia level is reasonable for unexplained ataxia with vomiting and encephalopathy. Lactate can also be considered. The typical reference range for ammonia is 15 to 45 μg/dL (11–32 μmol/L), but slight elevations are common due to variable collection techniques. However, any value greater than 100 μg/dL (>71 μmol/L) needs to be taken seriously; genetics should be contacted urgently to discuss further management. More generally, metabolic disease should be considered with unexplained relapsing ataxia or encephalopathy, particularly in the setting of fever or illness.

EVALUATION AND THERAPY

A thorough history and physical examination may make laboratory testing unnecessary, for example, with clear-cut migraine or ACA in a well-appearing child. At a minimum, however, urine toxicology should be considered. If there is a high clinical suspicion, blood and urine samples should be held with the intention of sending targeted analysis after consultation with poison control. Lumbar puncture should be considered in the setting of suspected infectious or inflammatory processes, including GBS. Either a normal WBC count or a mild pleocytosis in the CSF is typical in ACA. More significant pleocytosis or a low glucose level in the CSF raises the concern for bacterial meningitis or encephalitis, and an expanded evaluation for viral (especially herpes simplex virus) and bacterial causes is warranted.

Imaging of the brain is indicated in the presence of a focal neurologic finding on examination, or with the inability to perform a reliable neurologic examination in the presence of illness or sedation. Imaging in the absence of these indications is low yield. Acutely, head CT is effective for evaluating for hemorrhage or hydrocephalus. However, MRI of the brain spares the child irradiation and provides more sensitive visualization of the brain parenchyma. Additional studies with contrast are indicated if there is concern for infection and inflammation or tumor. Imaging of the vasculature with magnetic resonance angiography or magnetic resonance venography is useful when stroke is a consideration. Neurologic consultation should typically be obtained before ordering imaging to optimize the study, and before considering conventional cerebral angiography or CT angiography. Spinal cord MRI with and without contrast is useful to evaluate possible cases of ADEM, TM, and GBS. Enhancement of the lumbar roots or cauda equina is an important finding suggestive of GBS or other inflammatory or neoplastic processes in the appropriate clinical setting.

MANAGEMENT

Treatment Approach

Treatment is directed at the underlying diagnosis. Initial attention to vital signs in the ill child is crucial.

Posterior fossa hemorrhage requires urgent neurosurgical consultation. Ischemic stroke requires neurologic consultation and admission to a pediatric critical care unit for further management. In the case of ADEM, immune-modulating therapy, such as corticosteroids, IVIg, or plasma exchange can be considered: treatment can hasten recovery but does not seem to alter the ultimate outcome. A 2004 study of vestibular neuritis in adults found that vestibular function was improved in patients treated with methylprednisolone but not with valacyclovir. Infectious processes, such as cerebellar abscess or brainstem encephalitis, are treated initially with broad antimicrobial therapy (including ampicillin for *Listeria* in the case of brainstem encephalitis) as well as antiviral therapy (acyclovir for herpes simplex virus) until the causative agent is identified. Brain tumors require neurologic, oncologic, and neurosurgical consultation. GBS requires hospital admission for monitoring of vital signs and respiratory function. Treatment with IVIg or plasma exchange speeds recovery, and IVIg is favored because it is less invasive. IVIg should not be used in patients who are immunoglobulin A deficient.

Ongoing Care

Long-term treatment is not typically required for the common causes of pediatric acute ataxia. However, follow-up 2 to 4 weeks after hospital discharge to monitor recovery is reasonable. Prognosis and management are linked to diagnosis. If persistent or permanent dysfunction results, then therapy may require the coordination of physical therapy and sometimes adaptive medical devices. Aside from ingestion, few of the causes of ataxia are preventable. In most cases, the outcome is a good one. For patients requiring hospital admission, early recognition leading to early admission and treatment may improve outcomes.

Summary

- Based on observational studies and expert opinion, (3) for children 28 days to 18 years old with acute ischemic stroke presenting within the treatment window, tissue plasminogen activator should be considered.
- Based on case series and retrospective reviews, (7)(8)(24) acute cerebellar ataxia is typically a benign, self-limited condition. With typical presentation, in the postvaccine era, varicella is an unlikely cause. Lumbar puncture and magnetic resonance imaging of the brain are typically unrevealing and are, therefore, generally not recommended.
- Based on expert opinion, (11) acute disseminated encephalomyelitis should be treated with methylprednisolone, 10 to 30 mg/kg intravenously (IV) daily (maximum of 1 g IV daily), followed by a prednisone taper over 4 to 6 weeks. In severe or refractory cases, based on evidence from case series (12)(13), additional treatment with plasmapheresis or intravenous immunoglobulin (IVIg) should be considered.
- Based on case series and expert opinion, (9)(10) evaluation for occult tumor and treatment with immune therapy is recommended for opsoclonus-myoclonus syndrome.
- Retrospective evidence and expert opinion (19)(20) suggest that treatment of transverse myelitis with early corticosteroids improves outcome. When the diagnosis is being considered, early treatment with methylprednisolone, 30 mg/kg IV (maximum dose, 1 g IV), is recommended, even as other potential causes for acute myelopathy, such as epidural tumor and epidural hematoma, are being evaluated.
- Based on expert opinion, (22) Guillain-Barre syndrome treatment is typically with IVIg, 0.4 g/kg IV daily for 5 days. A multicenter trial of 95 children suggested that treatment hastens recovery and decreases relapse but does not clearly affect overall outcome (23).
- Based on multiple cohort studies (25)(26)(27) of acute flaccid paralysis due to enterovirus D68, empirical therapy with IVIg and/or corticosteroids has been ineffective.
- A randomized study of vestibular neuritis in adults found that vestibular function was improved in patients treated with methylprednisolone but not with valacyclovir (21).

References for this article are at http://pedsinreview.aappublications.org/content/40/7/332.

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1. A 7-year-old girl is seen in the emergency department for an unsteady gait. Which of the following findings on her neurologic examination is most likely suggestive of a vestibular dysfunction as the underlying cause of her ataxia?
    A. Dysdiadochokinesis.
    B. Horner syndrome.
    C. Lurching gait.
    D. Positive Romberg test.
    E. Pronator drift.
2. An 18-month-old boy is brought to the emergency department for an unsteady gait. He awoke in the morning and had difficulty sitting up on his own and refused to walk. He had been previously healthy apart from an upper respiratory tract infection approximately 1 week earlier. On physical examination he is afebrile, alert, well-appearing, and in no acute distress. His neurologic examination reveals truncal ataxia with difficulty maintaining a seated position and some intention tremor with reaching for objects. When placed on the floor to walk, he will cry and immediately sit down, refusing to walk. There is no nystagmus. Which of the following is the most likely diagnosis in this child?
    A. Acute cerebellar ataxia.
    B. Acute intoxication.
    C. Guillain-Barre syndrome (GBS).
    D. Opsoclonus-myoclonus syndrome.
    E. Posterior fossa tumor.
3. The emergency department physician makes the appropriate diagnosis in the patient in question 2 based on the clinical picture. Which of the following is the most appropriate way to counsel the family regarding the prognosis of this condition in this patient?
    A. At least 90% make a full recovery.
    B. His condition may progress to obstructive hydrocephalus.
    C. Less than 50% make a full recovery.
    D. Less than 50% will worsen, and the remainder will not make a full recovery.
    E. Prognosis depends on age at diagnosis, with patients younger than 2 years having a better prognosis.
4. The patient from the vignette in questions 2 and 3 returns to the clinic 4 weeks later for follow-up. His symptoms have not resolved. In addition, over the course of a month he has had some developmental regression and has been irritable, sleeping less, and less interactive with the family. On physical examination he is encephalopathic, remains ataxic, and now has emergence of rapid saccadic eye movements. Which of the following diagnoses must be considered at this point in this patient?
    A. Acute intoxication.
    B. GBS.
    C. Labyrinthitis.
    D. Opsoclonus-myoclonus syndrome.
    E. Posterior fossa tumor.

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5. An 8-year-old boy is seen in the emergency department for acute onset of ataxia. He also reports a "room-spinning" sensation and emesis. On evaluation he is ill-appearing and holding his head in his hands. Neurologic examination reveals prominent nystagmus, and he reports worsening of his vertigo with movement. He is unable to ambulate without falling over or feeling very nauseated. Which of the following is the most likely diagnosis in this patient?

   A. Acute cerebellar ataxia.
   B. GBS.
   C. Labyrinthitis.
   D. Opsoclonus-myoclonus syndrome.
   E. Posterior fossa tumor.

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