Acute Ataxia in Children: A Review of the Differential Diagnosis and Evaluation in the Emergency Department

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ABSTRACT

Acute ataxia in a pediatric patient poses a diagnostic dilemma for any physician. While the most common etiologies are benign, occasional individuals require urgent intervention. Children with stroke, toxic ingestion, infection, and neuro-inflammatory disorders frequently exhibit ataxia as an essential—if not the only—presenting feature. The available retrospective research utilize inconsistent definitions of acute ataxia, precluding the ability to pool data from these studies. No prospective data exist that report on patients presenting to the emergency department with ataxia. This review examines the reported causes of ataxia and attempts to group them into distinct categories: post-infectious and inflammatory central and peripheral phenomena, toxic ingestion, neurovascular, infectious and miscellaneous. From there, we synthesize the existing literature to understand which aspects of the history, physical exam, and ancillary testing might aid in narrowing the differential diagnosis. MRI is superior to CT in detecting inflammatory or vascular insults in the posterior fossa, though CT may be necessary in emergent situations. Lumbar puncture may be deferred until after admission in most instances, with suspicion for meningitis being the major exception. There is insufficient evidence to guide laboratory evaluation of serum, testing should be ordered based on clinical judgement—recommended studies include metabolic profiles and screening labs for metabolic disorders (lactate and ammonia). All patients should be reflexively screened for toxic ingestions.

Keywords: acute ataxia, cerebellar ataxia, toxic ingestion, Guillain-Barré syndrome, differential diagnosis, children, magnetic resonance, lumbar puncture

Introduction

Ataxia is a neurological disorder in which coordination of motor activity is impaired, preventing the execution of fluid movements. Children with ataxia classically present with an inability to ambulate as manifested by an ataxic gait, often described as a “wide-based gait” with “truncal instability.” Young children, especially, may manifest ataxia as a simple inabilty or refusal to ambulate. The key to assessment of acute ataxia in children is a thorough physical examination, which may reveal many possible associated findings and shed light on the location of the primary pathology. In this review, we present a broad differential diagnosis ranging from primary central causes to those secondary to infection or toxic exposure. We hope this will serve as a guide for physicians in the emergency department and consulting pediatric neurologists who are evaluating children presenting with acute-onset ataxia. The causes of ataxia can be organized in an anatomic fashion. Although an “ataxic gait” on examination is typically associated with cerebellar deficit, an abnormality in
gait can present as a consequence of deranged function in many locations along the central nervous system (CNS). Motor weakness can originate from a lesion in the cerebral cortex, brainstem, spinal cord, peripheral nerves, or neuromuscular junction. Impaired balance often results from dysfunction of the vestibular apparatus in the inner ear or the eighth cranial nerve.

A thoughtful history and physical examination technique will aid in localizing the source of dysfunction. Children who present with developmental delay or regression in milestones may suffer from a metabolic derangement such as an aminoaciduria (e.g., Hartnup and maple syrup urine disease), pyruvate dehydrogenase deficiency, or biotinidase deficiency. A prior ataxic event in an otherwise healthy child may suggest a paroxysmal disorder as is seen in genetic ion channel mutations (i.e., the “episodic” ataxias) or in complex migraines, in which the frequency and duration of attacks can vary widely between patients. Similarly, a previous history of extremity weakness or vision loss may indicate a polyfocal demyelinating disease such as multiple sclerosis (MS). Primary “infectious” or secondary “postinfectious” cerebellitis may be implied, respectively, with an either concurrent or recent viral syndrome, prompting the physician to elicit such a history and examine the patient for signs of rash.

Most disorders discussed herein demonstrate depressed mentation or speech abnormalities such as fluctuations in clarity, tone, rhythm, and volume. The cranial nerve examination may reveal a deficit, nystagmus, or palatal myoclonus. These patients may have hypotonia and their strength may appear diminished. Finger-to-nose may show under- or overshooting of the limbs. Patients may have difficulty with rapid alternating movements and intention tremor. Patients with peripheral neuropathies are usually hyporeflexive, conversely those with cerebellar insult may have pendular reflexes. Finally, gait testing may demonstrate poor maintenance of truncal position and titubation, or no ability to walk at all.

The temporal course of ataxia is diagnostically useful if acute toxic, traumatic, infectious, or postinfectious cases are suspected. Chronic or episodic ataxias, on the other hand, are generally the result of an inborn error of metabolism or hereditary channelopathies. Although an acute onset of ataxia has historically been associated with a benign course, it can present a unique challenge to physicians as a few possible causes can pose a real concern for irreversible neurological damage.

Only a handful of studies have documented the diagnoses one can encounter in children presenting with acute ataxia. Gieron-Korthals et al. in 1994 summarized 40 children who had been symptomatic for less than 48 hours and found a similar array of etiologies, providing support to the findings of Gieron-Korthals et al. Rudloe et al. in 2014 demonstrated that clinically significant intracranial pathology—tumors, infarcts, and acute disseminated encephalomyelitis (ADEM)—is frequently documented in children with symptoms up to seven days but is far less likely in young children with symptoms for less than 72 hours. Finally, Thakkar et al. in 2016 described 120 children referred to a pediatric neurologist with symptoms up to four weeks in which the leading diagnosis remained postinfectious in nature and the frequency of toxic ingestion was much lower than preceding studies had reported. The disparate conclusions that arise from these studies are rooted in their different design—all the aforementioned studies are retrospective—and each uses a different definition for the duration of symptoms as well as different inclusion and exclusion criteria.

Here we expand the differential diagnosis of acute ataxia into broad categories, as one might do with a patient presenting to care for the first time in the emergency department. We then discuss the clinical, laboratory, and imaging features reported with each entity, so that a clinician may be able to begin prioritizing their evaluation based on historical and examination features they may encounter. We give special attention to the evidence that supports the evaluation of acute ataxia in the emergency department to optimize the initial diagnosis, keeping in mind that ongoing evaluation and follow-up of these patients may require a different set of clinical tools and practices. We then summarize the different aspects of evaluation (history, physical examination, laboratory tests, imaging, and lumbar puncture [LP]) and give our recommendations. Finally, we hope this article will demonstrate the need for carefully designed prospective research to understand which circumstances might require close attention and swift action compared with those in which patients may be simply observed for a period of time.

Classification of etiologies

Central postinfectious and inflammatory causes

The most recognizable and generally most common causes of acute ataxia are postinfectious cerebellar processes that are self-limited and resolve spontaneously. The term “acute cerebellar ataxia” and each uses a different set of clinical tools and practices. We then summarize the different aspects of evaluation (history, physical examination, laboratory tests, imaging, and lumbar puncture [LP]) and give our recommendations. Finally, we hope this article will demonstrate the need for carefully designed prospective research to understand which circumstances might require close attention and swift action compared with those in which patients may be simply observed for a period of time.

Acute postinfectious cerebellar ataxia

The observation of a sudden-onset ataxia in children after an infectious illness was first documented for more than a century ago. As other causes for cerebellar dysfunction emerged, this remained a puzzling cause of ataxia for which the pathology remained unknown. Evidence for an autoimmune basis of APCA emerged with reports showing
invoking the subsequent use of cerebellitis to describe an
describing the same disease process.1,3 Horowitz et al. in
These earlier descriptions of the term did not differentiate it
oligoclonal bands in the cerebrospinal fluid (CSF), with
several subsequent studies demonstrating immunoglobulin G and immunoglobulin M reactive to cerebellar Purkinje
cells after varicella.14 Epstein–Barr virus (EBV),15,16 and
mycoplasma17 infections. However, the mechanisms underly­ing both the pathologic specificity to and the physio­logic disruption of the cerebellum are unknown.

Our best understanding of the epidemiology and outcome of APCA stems from work done by Connolly et al.,
the only group to have prospectively studied the disorder,
collecting data for more than a 23-year period. Of the 73
children who satisfied entry criteria, 19 (26%) had a priori
infection with varicella, two (3%) had EBV, and 36 (49%) had
a nonspecific “viral” prodrome, whereas 14 (19.2%) had no
identifiable prodrome. The latency period from infection to
ataxia ranged from only a few days to three weeks with a
mean between nine and 11 days for all but EBV infections,
which had a mean latency of 17.5 days. The mean age at
presentation was 5.37 ± 4.00, although the data are skewed
such that 60% of children are aged between two and four
years. Of 69 children who underwent LP, roughly half had
leukocytes less than 5/mm³ and all bacterial and viral
cultures were negative. Computed tomography (CT) was
unremarkable in all children imaged, whereas magnetic
resonance imaging (MRI) showed cerebellar T2 hyper­
intensity in only one of nine children imaged. Of the in­
dividuals who were followed, 70% returned to baseline
within eight months of initial presentation.8

Since the study by Connelly et al., one other retrospective
study with essentially similar results has emerged.19 How­
ever, without a good understanding of the pathophysi­ology of
the APCA, no tests are available to confirm the diagnosis.
The work of Connelly et al. shows us that the mainstays in
neurological diagnosis such as a thorough examination,
imaging, and LP are not specific either.

Whelan et al.4 and others19-21 favor a combination of a
normal mental status, a nonfocal neurological examination,
and a clear history of recent infection as reasons to defer
imaging or CSF studies for close neurological follow-up.
However, clear criteria do not exist that reliably exclude
concerning—although perhaps less common—diagnoses
that may require immediate intervention.

Postinfectious cerebellitis
The term “cerebellitis” appeared in the 1950s and 1960s
and was used interchangeably with cerebellar encephalitis,
a cerebellar syndrome in the setting of a recent infectious
disease such as infectious mononucleosis22 and varicella.23
These earlier descriptions of the term did not differentiate it
from APCA, and thus it is unclear whether they were
describing the same disease process.1,3 Horowitz et al. in
1991 documented a patient with severe ataxia and en­
cephalitis along with cerebellar edema on CT and MRI,24
invoking the subsequent use of cerebellitis to describe an
ataxia syndrome with the distinct feature of cerebellar
edema on imaging.25,26

Sawaishi and Takada27 summarized patients with post­infectious ataxia who had cerebellar edema with mass ef­
fect on imaging. Although these patients varied in severity
with a few mimicking APCA, many of them were life
threatening or fatal, necessitating surgical decompres­sion.25,26 Sawaishi and Takada thus argued the diagnosis of
acute cerebellitis should be reserved for severe cases with
positive imaging findings, with the implication that it
would convey an urgent need for surgical evaluation.

Desai and Mitchell28 in 2012 argued that cerebellitis and
APCA should be thought of as two ends of a spectrum, with
the former diagnosis being applied largely to cases with
cerebellar edema on imaging. However, Connelly et al.
demonstrated that mild cerebellar edema may occur in
children with ataxia who are otherwise well. In their study,
Thakkar et al. report three (2.5%) of 120 patients diagnosed
with acute cerebellitis, which they defined as the presence
of imaging abnormalities in the setting of acute ataxia—one
of the patients developed fulminant brain swelling
requiring decompressive occipital craniectomy. This
compared with 71 (59.2%) patients with symptoms and
normal imaging findings diagnosed with APCA.30

Our view of cerebellitis aligns with Sawaishi and Takada,
that it should denominate ataxia with the clinical distinc­tion
of an abnormal mental status to suggest increased
intracranial pressure and thus the need for immediate im­
aging. Without clear prospective data on the epidemiologic,
clinical, laboratory, or imaging features of cerebellitis, it will be
crucial to have a low clinical threshold for imaging and
surgical evaluation should a child begin to show signs of
altered mental status in the setting of a postinfectious
cerebellar ataxia. Although MRI may be more sensitive and
specific imaging compared with CT,26,30 CT may be neces­
sary in more clinically urgent scenarios.

**APCA, the clinically isolated syndrome, and MS**

APCA, the clinically isolated syndrome (CIS), and MS
describe three disease processes that have tremendously
overlap yet differ in their definition as delineated by specific
clinical and imaging features.31 All three are characterized
by polyfocal immune-mediated demyelinating lesions of
the CNS. The diagnosis of MS requires either evidence of a
prior demyelinating event or new lesions on imaging
follow-up, whereas CIS and ADEM are differentiated by the
presence of encephalopathy (Table).31,33

When evaluating a patient with acute ataxia, a history of
prior episodes of neurological deficit is important for
making the diagnosis of MS. However, a patient present­ing
with a first time demyelinating CNS event would—by sake
of the definition—be diagnosed with ADEM or CIS unless
MRI were to reveal evidence of an older (i.e., nonen­hancing)
demyelinating lesion.31 However, the diagnosis of ADEM or
CIS does not preclude a later diagnosis of MS. One study of
40 children initially diagnosed with ADEM or CIS demo­
strated that one of 15 children diagnosed with ADEM was
later reclassified as having MS, whereas 14 of 28 patients
with CIS had a relapse event, causing 13 of them to be
diagnosed with MS.34 The presence of oligoclonal bands in
the CSF may indicate a higher likelihood of relapse and
subsequent reclassification to MS.35

Although we do not wish to diminish the importance of
differentiating between these entities, further discussion of
a patient with demyelinating disease would likely occur
after imaging reveals the presence of lesions. Because CIS is a
relatively recent disease description that was first rigor­
ously defined in 200732 prospective studies have not yet
been published that identify the rate of ataxia as a pre­senting feature of the disease.
ADEM is an acute inflammatory demyelinating disorder that is generally preceded by an infection and affects the white matter tracts of the brain, brainstem, spinal cord, and optic nerves. The incidence is approximately 0.4/100,000 among children and a mean age 6.5 years, with 64% of patients aged between 2 and 10 years. The diagnosis requires polyfocal clinical CNS findings, encephalopathy not explained by fever, and demonstration of characteristic multifocal demyelinating lesions on MRI.

Ataxia is a common presenting feature of ADEM. In a prospective study spanning 12 years, 42 (50%) of 84 consecutive patients with ADEM presented with ataxia. Although it is unclear for how many patients ataxia was the only presenting feature, the study identified long tract signs in 71 (85%), hemiparesis in 64 (76%), and encephalopathy in 58 (69%) patients, of whom 16 progressed into a coma. Encephalopathy can be defined broadly as any change in mental status, as patients can present with irritability, sleepiness, confusion, or obtundation. It is important to keep in mind that because this study was published in 2002, the operational difference between ADEM and CIS had not yet been formalized to differentiate between patients with and without encephalopathy.

Of 82 patients prospectively included in the study by Tenembaum et al., MRI showed only small (less than 5 mm) lesions in 52 (62%), large confluent lesions were observed in 20 (24%), bithalamic involvement was seen in 10 (12%), and acute hemorrhagic lesions were seen in two patients. CSF studies were abnormal in 24 children (28%), showing either lymphocytic pleocytosis (more than 180 cells/mm³) or increased protein levels (more than 1 g/dL).

Classic ADEM should be easy to clinically differentiate from APCA, as it will typically involve focal neurological deficits along with a possible change in mental status concurrent with ataxia, both of which are generally indications for rapid imaging. However, the relative incidence of ADEM versus APCA is unknown, and no studies exist that allow us to clinically differentiate ADEM from other causes of acute ataxia. Although Martínez-Gonzáles et al. identified ADEM as the cause of ataxia in one of 39 patients studied, the relative incidence of ADEM compared with other causes of ataxia is otherwise unknown. For the wary clinician, a period of observation may be useful in determining an “illness curve” of how symptoms are progressing.

Nearly all patients will eventually demonstrate complete neurological recovery, although patients should be closely monitored for relapse. Although randomized controlled treatment trials for ADEM have not been performed, rapid initiation of high-dose intravenous methylprednisolone is a mainstay in treatment. However, some cases may be more severe, and stabilization of the patient may be necessary before diagnostic evaluation can be initiated: a fraction of cases will require intensive care unit admission as patients with ADEM have been shown to progress to fulminant brain injury and even death. Furthermore, approximately 17% of patients were prospectively shown to present with lesions in the brainstem that interfered with respiratory drive, necessitating prompt respiratory support. The administration of intravenous immunoglobulin in severe cases is not unwarranted, although its efficacy in treatment has not been prospectively studied.

### Definitions of MS, ADEM, and CIS Based on Clinical Findings and Imaging Findings as Described in Krupp et al. 2013

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<tr>
<th>Diagnosis</th>
<th>Clinical Findings</th>
<th>Imaging Findings</th>
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| MS        | (Any of the following):  
- Two or more nonencephalopathic clinical CNS events separated by more than 30 days  
- One nonencephalopathic episode with MRI findings that show DIS and follow-up MRI that shows DIT  
- One ADEM attack followed by a nonencephalopathic clinical event separated by ≥3 months with new MRI lesions  
- First, single, acute event that does not meet ADEM criteria and whose MRI findings demonstrate DIS and DIT | Demonstration of DIT and DIS |
| ADEM      | First time, polyfocal, clinical CNS event  
- Encephalopathy that is not explained by fever  
- Monofocal or polyfocal clinical CNS event  
- Absence of prior clinical evaluation of CNS demyelinating disease  
- No encephalopathy | Diffuse, >1-2 cm lesions of white matter  
- Absence of DIT  
- Absence of DIS  
- Absence of DIT or DIS |
| CIS       | Monofocal or polyfocal clinical CNS event  
- Absence of prior clinical evaluation of CNS demyelinating disease  
- No encephalopathy | |

**Abbreviations:**
- ADEM = acute disseminated encephalomyelitis
- CIS = clinically isolated syndrome
- CNS = central nervous system
- DIS = dissemination in space
- DIT = dissemination in time
- MRI = magnetic resonance imaging
- MS = multiple sclerosis

Definition of DIT and DIS from Polman et al., 2010.

**TABLE:** Demonstration of DIT and DIS from Polman et al., 2010. DIT: a new T2 or contrast-enhancing lesion on follow-up MRI with reference to baseline or the simultaneous presence of enhancing and nonenhancing lesions at any time. DIS: at least one T2 lesion in two of the following four areas of the CNS—periventricular, juxtacortical, infratentorial, and spinal cord.
GBS, an idiopathic, postinfectious inflammatory disorder of the peripheral nerves. The spinal and peripheral postinfectious phenomena are a series of immune-mediated disorders including GBS, Miller Fisher syndrome (MFS), and Bickerstaff brainstem encephalitis (BBE). Although these syndromes are often thought to be distinct, they frequently overlap in their features with ataxia being a major component of their clinical presentation. The nonspecific finding of anti-GQ1b and anti-GM antibodies in the serum of affected patients suggests GBS, MFS, and BBE are variants of a single disease process.54,55 The classical association with antecedent campylobacter infection is also bolstered by the association between the organism and anti-GM1 antibodies.43 Transverse myelitis, with its associated disorders, is also discussed in this section as a cause of acute ataxia.

Guillain–Barré syndrome

GBS is a postinfectious polyneuropathy that can affect individuals from 12 months into adulthood, with a peak incidence at five to six years.46 Patients generally present with symmetric lower extremity weakness and areflexia—the two major defining criteria for GBS diagnosis.47 A small percentage of patients (less than 5%) may present with normal or exaggerated reflexes.48 Autonomic instability may also occur, resulting in heart-rate variability and cardiovascular collapse.49

Several minor criteria aid in differentiating GBS from other causes of ataxia. For example, a prospective study showed that 85% of adult patients with GBS complained of pain on admission.50 Another prospective study by Paradiso et al.51 showed 44 of 61 (72%) children with GBS complained of pain, although it is unclear whether pain was part of the initial presentation or if it appeared later on in the course of illness. Another retrospective study found that children greater than five years of age with GBS were more likely to initially complain of limb pain (53%) than their younger counterparts (24%).52

A characterizing feature of GBS is increased protein levels in the CSF with albuminocytologic dissociation, meaning that the cell counts are typically normal despite an increased protein level.53 Although we intuitively realize this is an important test for diagnosing GBS, CSF protein levels are commonly normal in the first week of presentation. Early work by Ropper54 demonstrated that only 50% of patients initially presented with CSF protein greater than 0.55 g/L. A more recent prospective study conducted by Nishimoto et al.44 showed only 44% of patients with GBS have abnormal protein levels in the first week of illness.

Published European guidelines for the diagnosis of GBS argue that CSF studies are of very limited value, and the diagnosis should usually be made on clinical grounds alone.55 Our view is that, although CSF studies may be useful in characterizing the course of disease and subsequent response to treatment, they may be deferred until after the patient is admitted from the emergency department as they will rarely direct immediate management.

Imaging is not a part of diagnostic criteria in GBS and can be deferred in cases with little clinical ambiguity.56 However, as there can be overlap with MFS and BBE, which can respectively involve the cranial nerves and brainstem, MRI may be a diagnostic necessity. Zuccoli et al.57 gathered retrospective neuroimaging data on 17 patients who presented with clinical GBS, of whom 14 (82%) showed enhancement of the cauda equina.

Most patients who are adequately treated with immunomodulatory therapy will generally recover their neurological function within the first year after the initial presentation.58 However, as with most postinfectious disease, GBS presents within a spectrum of varying severity where approximately 13% of children will progress to respiratory failure requiring ventilator support.51

Miller Fisher syndrome

Although the most common form of GBS involves ascending paralysis in the extremities, several variant forms have been described, which often involve prominent cranial nerve involvement. MFS is one such variant, which also differs from typical GBS, in that it tends to have a more rapid onset and greater severity.59 Although MFS is strongly associated with the clinical triad of ataxia, areflexia, and ophthalmoplegia, it is important to note that any ascending polyneuropathy can present with dysfunction of any of the cranial nerves. One study prospectively found that of all children presenting with GBS-like symptoms such as lower extremity weakness and areflexia, 27% also presented with cranial nerve dysfunction and another 46% developed some kind of cranial nerve dysfunction during the course of hospitalization.60

Ancillary testing plays a similar role with MFS as it does with GBS. CSF shows increased protein levels in 25% of patients during the first week of presentation, again suggesting the limited role of LP in the initial evaluation of MFS.64 As discussed previously, the presence of anti-GQ1b antibodies is highly suggestive of MFS but has also been shown in polyneuropathies that do not have cranial nerve involvement.45

Bickerstaff brainstem encephalitis

BBE is a relatively obscure medical condition described as a clinical triad of ataxia, ophthalmoplegia, and a “disturbance of consciousness.”65 It is generally characterized as occurring with an antecedent history of infection, albuminocytologic dissociation in the CSF, and anti-GQ1b antibodies in the serum.45 One group delineated criteria as being “definite” when ophthalmoplegia, ataxia, and impaired consciousness are present in the setting of positive serum anti-GQ1 antibodies and the absence of other excludable conditions.61

A nationwide survey of Japanese physicians was conducted to collect data on all patients with likely BBE between 2006 and 2009. Thirty-seven patients were found to fulfill criteria for either definite (19) or probable (18) BBE. Of these, 54% presented with limb weakness and 67% with absent or decreased reflexes. Ninety-two percent of patients presented with ataxia, 100% with ophthalmoplegia, 41% with facial palsy, and 72% with oropharyngeal palsy. Laboratory investigation showed normal CSF cell counts (less than 5/mm³) in 56% and normal protein (less than 45 mg/dL) in 62% of patients. Brain MRI was abnormal, showing T2 hyperintensity of the brainstem, thalamus, and cerebellum in eight (23%) of 35 patients. Patients were treated with
immunologic therapy—intravenous immunoglobulin (92%), steroid (49%), or acyclovir (24%)—with 91% of patients able to walk independently at one-year follow-up.61

There is speculation that BBE is under-reported because it is not widely recognized as distinct from GBS or MFS.62 Although data on the disorder are scarce, one series documented several patients with clinical brainstem lesions who had simultaneous motor axonal neuropathy on electrodiagnostic studies suggesting a clinical overlap with GBS.60 The shared finding of serum anti-GQ1 antibodies provides further evidence of shared etiologic factors.45

BBE presents an interesting diagnostic problem, because imaging and LP appear to have little utility as with all other postinfectious phenomena discussed so far. The challenge presents itself with the presence of lesions that clearly localize to the brainstem, which would be a certain indication for imaging. Our view is that BBE may serve as a diagnosis of exclusion in the face of cranial nerve abnormalities with negative imaging findings.

Transverse myelitis

Acute transverse myelitis (ATM) is a rare focal inflammatory disorder of the spine that affects one to four in every million persons per year, with a bimodal age distribution between the ages ten and 19 years and 30 and 39 years.63 The Transverse Myelitis Consortium Working Group outlined a diagnostic algorithm in 2002, which included muscle weakness with upper motor neuron signs and sphincter dysfunction with a clear sensory level. With this clinical suspicion, the recommendation is to obtain a contrast-enhanced MRI within four hours to rule out compressive myelopathy, which may necessitate a surgical evaluation or a course of intravenous methylprednisolone.63

Idiopathic ATM—the isolated and monophasic form of the disease—was retrospectively studied in children of a period spanning 23 years. Of 27 patients studied, ten (39%) had an antecedent infection and 20 (74%) presented with paraparesis. The mean age of onset was 9.5 ± 5.7 years. Although ataxia is not explicitly stated as a clinical feature, a sudden onset of paraparesis would present with an inability to walk, which in younger individuals might be difficult to distinguish from cerebellar ataxia. CSF pleocytosis was seen in ten (37%) and increased protein levels in 12 (44%) patients. Imaging revealed T2 hyperintensity most often in the gray matter of the cervical and thoracic spine. Although surrounding white matter was occasionally involved, isolated white matter lesions were not seen. Of 21 patients who were imaged with MRI, seven (33%) had multifocal lesions whereas six (28%) showed no abnormalities, although some of these data may have been collected with older, less sensitive, imaging techniques.64

Although ATM can occur as a postinfectious process, it is also known to be a rare feature in several connective tissue disorders (sarcoidosis, Behçet’s disease, Sjögren’s syndrome, systemic lupus erythematosus, and so forth) and is also a common first presentation of MS.65 The presence of optic neuritis will suggest either neuromyelitis optica or MS as the underlying etiology. All cases of ATM eventually require CSF studies to examine for specific markers of disease, although these tests do not need to be immediately done.65 A discussion on diagnosing the different causes of ATM is out of the scope of this review, as it would likely be done after imaging is performed and the patient is admitted from the emergency department.

Toxic ingestion

Toxic ingestion is a common problem in the pediatric population. In 2013, 1.3 million children aged less than 19 years in the United States were reported to poison control centers for accidental and intentional ingestion of prescription and nonprescription medications—78% of victims less than six years of age.65 Medication ingestion in children accounted for an estimated 9490 emergency hospitalizations between 2007 and 2011, 75% of which were children either one or two years of age. Benzodiazepine ingestion accounts for approximately 10% of these patients, representing one of the most frequent classes pharmaceutical agents to be ingested.67 Although major efforts are currently being made to introduce safer packaging for commonly ingested pharmaceuticals,68 toxic ingestion remains an important cause of ataxia.

Gieron-Korthals et al. showed that approximately one third of acute ataxia in children resulted from toxic ingestion. Although benzodiazepines were the most common offender, phenytoin, phenobarbital, and carbamazepine were also important substances identified by the study.7 Martinez-González et al.7 reported dextromethorphan and ethanol to as two other toxic causes of acute ataxia. New studies are needed to evaluate which substances are currently implicated in acute ataxia, as the incidence of poisonings may have changed for more than the past 20 years.

Benzodiazepines

Benzodiazepines are one of the most commonly ingested substances by children and have been repeatedly published

![FIGURE 1](Image)

Relative rates of benzodiazepine, carbamazepine, and phenytoin ingestion in children aged less than six years. The comparison between 2009 to 2013 and 1988 to 1992 is made to highlight the relative reduction of carbamazepine and phenytoin ingestion juxtaposed with the relative increase in benzodiazepine ingestions in the time since Gieron-Korthals et al. published their study on the causes of ataxia. Patients greater than six years of age could not be compared, because the age ranges used to categorize the data had changed between the two periods of time.
as a frequent cause of acute ataxia.\textsuperscript{4,7,8,11} An average of 10,000 ingestions per year occur in children.\textsuperscript{59-71} Clinical features include lethargy advancing to coma, with respiratory depression as an important feature to be aware of.\textsuperscript{72} Although the sedative effects of many substances can cause pupillary constriction,\textsuperscript{73} benzodiazepines have been shown to not affect the pupil size in the same way opiates might.\textsuperscript{74} Amnesia and diplopia are two other features that have been described in the dental literature.\textsuperscript{75}

The landmark 1994 study by Gieron-Korthals et al. demonstrated that only five (12.5\%) of their 40 patients with acute ataxia had ingested benzodiazepines, yet that group represented the most cases of ataxia attributed to a single drug class.\textsuperscript{7} Data collected by the American Association of Poison Control Centers show that, in children less than six years of age, benzodiazepine ingestion rates are higher in recent years compared with the time period when Gieron-Korthals et al. collected their data (Fig 1).\textsuperscript{69,70,76,78-82} The reason for this sharp decline is ten-fold less than in the five years preceding their publication,\textsuperscript{59-71,76-82} which may also be in part because of a reduction in phenytoin prescriptions.\textsuperscript{85}

**Antiepileptics: carbamazepine and phenytoin**

Gieron-Korthals et al. reported that, apart from benzodiazepines, carbamazepine and phenytoin were the two antiepileptic drugs (AEDs) most commonly implicated in acute ataxia. Three of their 40 patients had ingested phenytoin and two had ingested carbamazepine.\textsuperscript{7} A retrospective study by Lifshitz et al. reported ataxia in slightly less than one third of children with carbamazepine poisoning, with clinical improvement seen in all patients. Nystagmus is the most common presenting feature, and although ataxia may be seen as a more concerning symptom, the combination of the two may suggest carbamazepine poisoning.\textsuperscript{83}

Carbamazepine ingestions have also decreased in the past 20 years, most notably in children aged less than six years (Fig 1).\textsuperscript{59-71,76-82} This finding coincides with a generally reduced prescription rate of carbamazepine, and the increasing use of newer AEDs.\textsuperscript{84,85} Oxcarbazepine, a newer generation AED with a similar mechanism of action, has been shown to have more benign toxic profile in overdosing, which does not seem to include ataxia, although dizziness and vertigo is a feature in about 1\% of cases.\textsuperscript{86}

Phenytoin toxicity is also classically associated with ataxia, often in conjunction with vertical downbeat nystagmus and vomiting.\textsuperscript{87} Gieron-Korthals et al. described three patients with acute ataxia who were ultimately found to have overingested phenytoin.\textsuperscript{7} However, average phenytoin ingestions for more than the past five years are ten-fold less than in the five years preceding their publication,\textsuperscript{59-71,76-82} which may also be in part because of a reduction in phenytoin prescriptions.\textsuperscript{85}

**Cough syrup: dextromethorphan**

Dextromethorphan is the main ingredient in widely available over-the-counter cough suppressants with CNS adverse effects that makes it a popular drug of abuse.\textsuperscript{88} Different effect “plateaus” have been described in which increasing concentrations of dextromethorphan will lead to distinct symptoms: euphoria (2.5 mg/kg), imbalance and visual sensations (7.5 mg/kg), altered consciousness and delayed reaction times (15 mg/kg), hallucinations, ataxia, and complete dissociation (greater than 15 mg/kg).\textsuperscript{99}

One 30-month-old child with an approximate 38 mg/kg ingestion of dextromethorphan presented to the emergency department with opisthotonos that resolved with administration of diphenhydramine, although the patient demonstrated ongoing ataxia and nystagmus until the next morning.\textsuperscript{90} It is important to recognize that although some over-the-counter formularies contain dextromethorphan as its only active ingredient, other products may also contain pseudoephedrine, which may induce irritability and hyperactivity in a child superimposed on ataxia and nystagmus.\textsuperscript{91} Fortunately, the rate of cough syrup ingestions has been rapidly declining for more than the past five years (Fig 2).\textsuperscript{59-71,76} Data are needed to determine the incidence of cough syrup ingestion as a cause of acute ataxia.

**Ethanol**

Ethanol toxicity can present with a range of mental status changes and respiratory depression, with children often at a risk of hypothermia and hypoglycemia.\textsuperscript{92} Ethanol is well-documented cause of cerebellar dysfunction, although the mechanism is not fully understood.\textsuperscript{93} Research in animal models has shown that adolescents have a higher threshold to motor dysfunction compared with adults,\textsuperscript{94} although a similar dose-dependent relationship has not been shown in humans. Other than the single patient retrospectively identified by Martínez-González et al.\textsuperscript{9} from a group of 39, the rate of ataxia in children with ethanol ingestion has not been studied; therefore the blood concentrations of ethanol needed to generate ataxia are unknown.

There appears to have been a large reduction in childhood ethanol ingestion for more than the last several years. The American Association of Poison Control Centers’ National Poison Data System documented 22,137 ethanol ingestions in 2009, 72\% of which were children less than six years of age who ingested nonbeverage ethanol. This number dropped to 7,093 after two years, and in 2013 was 5,839 (Fig 2).\textsuperscript{69-71,76} The reason for this sharp decline is...
unclear, although one possible explanation is a trend away from the sale and home-use of alcohol-based mouthwash. Whether this trend is the reason for fewer childhood alcohol ingestions or has had an appreciable effect on the rate of ataxia in children is unknown.

Marijuana

Ataxia can be a result of marijuana use, which usually occurs in adolescents participating in risky behavior. However, young children presenting with ataxia, tachycardia, and vertical and horizontal nystagmus have been documented to have cannabinoids in their serum. Marijuana and the many synthetic cannabinoids are known to have a wide range of toxidromic features: patients initially believe a sense of euphoria, but can progress to paranoia, delusions, hallucinations, panic attacks, nausea, vomiting, seizures, and dizziness.

The rate of reported ingestions of marijuana and cannabinoid-containing edibles has steadily increased in the past five years, especially in children less than six years of age (Fig 2), suggesting that they may be important considerations as the cause of acute ataxia in the face of the increasing liberalization of these substances. A thorough history should include the presence of these substances in the household, including inhaled and edible forms. Marijuana is commonly baked into cookies or brownies, which has been shown to be a cause of accidental ingestion in children leading to coma. Cannabinoids may not be routinely tested as part of toxicology screens; thus it is important to actively

Figure 2.
Rates of reported ingestions of different substances known to cause ataxia in children. Data gathered from the Poison Control Centers’ National Poison Data System.
consider marijuana toxicity in the differential diagnosis of acute ataxia.

**Cerebrovascular**

Childhood stroke is an extremely rare but devastating event, with cerebellar involvement occurring in an even smaller subset of this group of patients. There are documented examples of both hemorrhagic and non-hemorrhagic cerebellar stroke in children, with listed outcomes ranging from complete recovery to permanent neurological dysfunction and occasionally death. In such individuals, intervention must be initiated early to achieve optimal outcomes. Ataxia can be a major presenting feature for these children, and although rare, early diagnosis is critical. Although we do include case reports and case series in this section, there is a knowledge gap in understanding how acute ataxia may be the initial presentation of stroke. Further study is needed to help in differentiating stroke from other causes of ataxia, as it is one of the etiologies that can be missed when there is much to gain from rapid intervention.

**Hemorrhagic**

Intracranial bleeding is a medical emergency, necessitating prompt imaging and neurosurgical evaluation. A retrospective study documented four children with cerebellar hemorrhage that presented with acute-onset ataxia. For these patients, other neurological signs and symptoms were highly variable and occasionally absent. Headache was a common accompanying symptom, where the timing ranged from sudden onset to progressive for more than the course of three days. The GCS for these patients was normal in all except one. Cerebellar hemorrhage in children was frequently found to reveal underlying cavernous angioma or an arteriovenous malformation in the posterior fossa. Although these conditions may require eventual surgical correction, the need for immediate surgical intervention is dictated by the extent of fourth ventricle effacement and a GCS less than 13. Although most neurosurgical outcome data are from studies done in adults, childhood does not appear to significantly influence indications for surgery.

Headache appears to be the most frequent accompanying symptom, and is an indication for rapid imaging in children who describe their headache as being "unusual," "sudden," or "worst." A GCS less than 13 is also an important indication for imaging, with rapid imaging preferable over sensitive imaging. Rapid MRI protocols allow a time in the scanner (“table time”) that is comparable with that of rapid CT scanning, although its use in children has only been studied in its ability to assess for ventriculoperitoneal shunt malfunction. Furthermore, its use in emergency settings has been limited to retrospective studies. As a result, the sensitivity of rapid MRI protocols in detecting intracranial pathology in the posterior fossa cannot reasonably be inferred and remains to be elucidated. Evidence of hemorrhage in the posterior fossa in children less than three years of age may alert the physician to nonaccidental trauma.

**Nonhemorrhagic**

Acute ataxia can be the result of an ischemic cerebellar insult resulting from an occlusion in the posterior circulation. Ischemic stroke in the brainstem is uncommon. One review documented 36 published examples of vertebral artery dissection (VAD) in children for more than a span of ten years. Another review of posterior circulation stroke in children indicated that slightly less than half of cases were attributable to VAD. In the Gieron-Korthals et al. report, only one of the 40 patients identified in a ten-year interval had a cerebellar infarction, and this individual was not described in detail.

Posterior circulation ischemic stroke can occur at any age. Hasan et al. suggested that about half of children with VAD present with ataxia and that half of the patients have no clear history of trauma to the head or neck region. Impairment of consciousness occurs in a third of the patients. After ataxia, headache and vomiting were the two most common presenting symptoms, each occurring in 38% and 34% of cases, respectively. Neurological examination showed a deficit in the visual system in 72% of cases, manifesting as either nystagmus, visual field deficits, ptosis, pupillary abnormality, or abducens (sixth) nerve palsy. Furthermore, 54% of cases occur with gross motor deficit manifesting as either hemiparesis, hemiplegia, or quadriplegia.

Hasan et al. reported abnormalities in CT angiography for all the cases they identified. Only ten of 63 children had signs “pathognomonic” for VAD, showing either an intimal flap (six) or eccentric filling defect (four) in the vertebral artery. The remaining 53 cases had signs “highly suggestive” of VAD, including occlusion, pseudoaneurysm, irregularity, stenosis, narrowing, thrombosis, or a “string of beads” appearance suggestive of fibromuscular dysplasia. With the low pretest probability of VAD in children, however, it is important to be cautious in interpreting abnormal results. Without data on the rate of these findings in asymptomatic children, the positive predictive value for such highly suggestive findings is unknown.

A retrospective cohort study at Boston Children’s identified three of 364 children presenting to the emergency department with ataxia duration of less than seven days who had a cerebellar infarct. Of the three patients identified in this study, MRI provided the standard of imaging, whereas CT failed to identify an abnormality in one of the cases.

**Venous sinus thrombosis**

Cerebellar venous infarction can occur as a result of isolated venous sinus thrombosis (VST) in the posterior fossa, accounting for about 2% to 4% of all intracranial thromboses. One study by Ruiz-Sandoval et al. uncovered nine patients that presented with isolated cerebellar venous infarction. Of these patients, all except one presented with ataxia, with seven complaining of dizziness and seven with a depression in mental status (ranging from drowsiness to coma). Three patients were aged 14, 15, and 18 years, with all of them found to have an underlying coagulopathy (puerperium and protein C deficiency).

CT is insensitive and nonspecific in diagnosing cerebellar VST, and MRI with magnetic resonance venography proves to be the diagnostic study of choice. Kulkarni et al. showed diagnostic findings in three of five patients imaged, with MRI detecting the venous abnormality in the remaining two. Ruiz-Sandoval et al. reported CT as showing...
abnormalities in all patients studied (hypodensities, mass effect, and hydrocephalus), although in none of the patients was VST detected. MRI was abnormal in all patients assessed, with the VST and cerebellar involvement detected in all cases. These data included adolescents and adults, so their validity for younger individuals is unclear.

**Infectious**

**Meningitis**

Meningitis is commonly included in the differential diagnosis of acute ataxia, with one group advocating for LP in children who have altered mental status and negative CT findings to rule out meningitis. Bacterial meningitis is a serious life-threatening infection of the meningeal membranes that demands rapid diagnosis and subsequent treatment with antibiotics. Thompson et al. described the onset and time course of clinical signs and symptoms in 544 children, teasing out that fever, sepsis features, hemorrhagic rash, impaired mental state, and meningism and the main features that appear within the first 48 hours of disease. A systematic review of prospective data further characterized the sensitivity and specificity of 26 different signs and symptoms seen with bacterial meningitis. Neither study mentions ataxia as an important presenting feature of disease.

A 1972 series described four children with bacterial meningitis who presented with ataxia as a major feature of illness. All had elevated temperatures and three exhibited altered mental status. Gieron-Korthals et al. included one child with acute ataxia and viral meningitis; this patient’s clinical details are not described in detail but there was CSF pleocytosis. Thalkkar et al. mentioned one patient with ataxia and meningitis, but they did not specify whether it was bacterial or viral and did not include the CSF findings.

Bacterial meningitis is an unlikely cause of acute ataxia, especially in a child without the classic features of fever or meningismus. Furthermore, the introduction of the Haemophilus influenzae type-b and conjugate Pneumococcal vaccines has dramatically reduced the incidence of bacterial meningitis in the United States to approximately 200 cases per year, at a mean age 0.6 (0.2 to 4.0) years. However, culture-negative (i.e., aseptic) meningitis remains a common occurrence that is difficult to clinically distinguish from bacterial meningitis. A close examination of the rate of meningitis in the setting of acute ataxia is critical for determining the diagnostic utility of LP in the emergency department.

**Rhombencephalitis**

Rhombencephalitis is an extremely rare manifestation of disseminated listeria or varicella infection, which has been reported predominantly in immunosuppressed adults. In one case series of adults with Listeria rhombencephalitis, ataxia was shown in 27% of patients in whom fever was universally present with meningismus in 64% of patients. All patients with CSF studies were shown to have pleocytosis, CT was positive in only eight of 21 patients. One report documented lesions in the brainstem and cerebellum on MRI.

Enterovirus 71 is a cause of hand, foot, and mouth disease that can have devastating neurological sequelae and is notorious for a 1998 epidemic in Taiwan leading to the hospitalization of 320 children with neurological disease, of whom 55 died. A total of 41 of these patients were studied, of whom 37 (90%) had rhombencephalitis, 20 (54%) of which had grade I disease characterized by myoclonus with either tremor or ataxia or both. Seven (19%) had grade III disease, which entails fulminant neurogenic pulmonary edema because of rapid cardiopulmonary failure. Despite mechanical ventilation and cardiopulmonary support, five of these patients died. Milder forms of rhombencephalitis were varied in their clinical presentation, although none presented with changes in mental status. MRI showed lesions restricted to the brainstem and not affecting any supratentorial tissue. A treatment for enteroviral rhombencephalitis has not been proposed other than to provide appropriate supportive care.

**Labyrinthitis**

Labyrinthitis refers to the neurological manifestations of otitis media, usually as a result of bacterial toxins or host inflammatory mediators migrating into the inner ear without invasion of bacteria per se. Although older children will usually report vertigo to their parents, younger children who are unable to verbalize their complaint may appear to have ataxic gait. Although it is a very unusual cause of ataxia, a clinical evaluation of otitis media should raise suspicion for this condition. Children stereotypically present with nausea and vomiting, along with nystagmus.

Gieron-Korthals et al. and Martínez-González et al. did not attribute ataxia to labyrinthitis in any of their patients. MRI is the most sensitive means of detecting labyrinthitis, with the affected cochlea showing contrast enhancement. Symptoms typically resolve with antibiotics, although a child with multiple occurrences should be evaluated by otolaryngology.

**Miscellaneous**

**Opsoclonus-myoclonus syndrome**

Opsoclonus-myoclonus syndrome (OMS) is commonly associated with occult neuroblastoma, although historically the failure to recognize the syndrome has led to a delay in diagnosing the tumor by more than a year after initial presentation. Thalkkar et al. noted that 10 (8.3%) of their 120 patients had OMS, although the clinical details of these cases are otherwise unreported. A prospective survey in the United Kingdom identified 19 individuals with OMS, two of whom presented with acute ataxia. In this study, mean age of presentation was 18 months, and the children presented with a combination of ataxia, opsoclonus (chaotic conjugate eye movements often referred to as “dancing eyes”), and irritability. LP was abnormal in one of 10 patients, showing an unspecified pleocytosis.

The prevalence of neuroblastoma in individuals with OMS has increased during the last several decades, probably due to a combination of improvements in imaging and an increasing recognition of the disorder. A retrospective study of OMS showed a diagnostic prevalence of neuroblastoma in 43% of patients evaluated in 2000. The diagnostic focus
with OMS has thus transitioned to excluding the presence of occult neuroblastoma.125

Urine catecholamines have only a 24% sensitivity in diagnosing neuroblastoma in the presence of OMS.125 Although significantly increased numbers may help guide diagnosis, further investigation for neuroblastoma is better deferred for a time after the acute evaluation in the ED, either when the patient has been admitted or in clinical follow-up if the symptoms of ataxia do not subside.

Celiac disease

Celiac disease is an autoimmune disease triggered by gluten ingestion. Its onset can be at any age, and children typically present with vomiting, diarrhea, constipation, and abdominal pain with infants often demonstrating failure to thrive.126 Gluten sensitivity has been associated with ataxia, with one series demonstrating 16 of 48 children presenting at the onset of their celiac disease with one or more neurological symptoms—two children presented with cerebellar ataxia and had cerebellar atrophy on CT, although it is unclear what the timing of symptoms was.127 A different study, however, prospectively followed 835 children with gluten sensitivity, defined as any child with gluten sensitivity-associated antibodies in their sera and positive intestinal biopsy. This study showed no children with ataxia or other cerebellar manifestations, with only a slightly higher incidence of neurological manifestations compared with control subjects.128 In one small series of patients with “gluten ataxia,” 12 of 13 patients showed antibodies in their sera that bound to Purkinje cells in rat tissue, suggesting a pathologic basis for the association.129

The association of ataxia in children with celiac disease is controversial and poorly studied. No individuals with gluten ataxia were documented in either the Gieron-Korthals et al.7 or Martínez-González et al.8 series of acute ataxia.

Pseudoataxia

The final diagnosis we will discuss is ataxia of a nonorganic nature, or pseudoataxia. Gieron-Korthals et al.7 described one patient in their retrospective cohort as having had a “conversion reaction,” but detailed clinical features were not included. Many such terms are encountered in the medical field that imply a nonorganic disorder, among them are “dissociative,” “functional,” “somatoform,” “psychogenic,” “supratentorial,” “hysterical,” and “medically unexplained.” A gait disorder of this nature is often referred to as an “idiopathic” gait disorder.

One study evaluated 103 children with acquired gait disorders, eight of whom had idiopathic ataxia amounting to an estimated incidence of 2.9 per 1,000,000 children. Of these eight children, five were female and three were male, and they ranged between ten and 15 years of age. All children with idiopathic gait disorder had significant school absence and were scholastically above average before their illness. Most of these children had many laboratory investigations completed, including six patients who had MRI of either brain, spine, or both, and five who underwent electroencephalography.130

Although laboratory and imaging investigations are normal in this situation, there are no validated methods with which a physician could diagnose pseudoataxia. One opinion piece offers clinical methods for detecting functional gait disorders in children, such as an age-appropriate cognitively challenging task when walking.131 Although these methods may intuitively make sense, their sensitivity and specificity in detecting functional gait disorders have not been studied and are thus unknown.

Evaluation of acute ataxia

Evaluating a child with acute ataxia is challenging, especially in the absence of clear guidelines to direct clinical management. Physicians in the emergency department are faced with the dilemma of obtaining imaging or spinal fluid or deferring such testing for the wards. Until recently, the only two studies that have examined all patients who presented with acute ataxia are those by Gieron-Korthals et al.7 and Martínez-González et al.,8 both of which were retrospective and only included approximately 40 patients.7,8

As initially discussed, one cannot undervalue the utility of careful history taking and physical examination skills in evaluating a child with acute ataxia. More often than not, a straightforward cause of ataxia can be derived without ancillary testing. However, the presence of lateralizing findings on neurological examination poses a real concern for acute intracranial pathology that must be aggressively investigated.

The current literature offers some guidelines on the evaluation of ataxia based on features of the clinical evaluation and examination, but the positive and negative predictive values of clinical findings rarely play a role in guiding testing. Furthermore, the sensitivity of certain testing will play a major role in deciding which tests to order, or whether to continue testing in the face of negative findings. In this section of our review, we cover the differentiation between patients with isolated ataxia or those with concurrent altered mental status as well as the role of ancillary testing in the emergency department for a child presenting with acute ataxia.

The history

The sudden onset of ataxia can be very distressing to parents and patients alike. It is important that the provider elicits much of the history by thorough questioning, as the patient or their caretakers may not be able to associate prior events with the current presentation. For the most acute cases in which there is concern for an evolving intracranial process or where the child is medically unstable, a brief history should include the presence of any other symptoms, known allergies, current medications, past medical history, last oral intake, and events leading up to the presenting symptoms. In such scenarios, it may be appropriate to forgo detailed history taking for the sake of triage and timely intervention.

The timing of symptoms can be helpful in narrowing the differential. Ataxia evolving for a period of less than 72 hours is unlikely to be of neoplastic origin.7,8 The presence of an infectious syndrome or vaccine administration as far as 2 weeks before presentation may implicate one of the many postinfectious phenomena as the cause of ataxia. Any associated trauma to the head and neck is important to note.
and merits thorough examination, close monitoring, and potentially imaging.

Hemiplegic ataxia caused by weakness in the postictal state has been described, although it has not been seen in any studies evaluating the different causes of acute ataxia in children. Nevertheless, a history focused on the possibility of epilepsy is important in ambiguous cases as these patients stand to benefit greatly from early diagnosis and intervention. A prior history of intermittent paroxysmal headaches—which caregivers may believe is not relevant to a new onset of ataxia and thus may not readily offer—may indicate complex migraine or hemiplegic migraine as the causative entity. Recurrence of ataxia in an otherwise undiagnosed patient should raise suspicion for migraine and seizures as the causative diagnosis. On the other hand, a headache that is sudden in onset or described as the “worst headache of my life” should trigger suspicion for hemorrhage. Any unclear or inconsistent history that is concerning for nonaccidental trauma should be taken seriously, as patients must carefully articulate individually spoken syllables. Finger-to-nose and heel-to-shin can be used to detect dysmetria, a sign indicating ipsilateral cerebellar damage. Reflex testing of the knees may demonstrate a “pendular” response, in which the leg swings more than four times after the tendon is struck. Finally, gait testing may reveal a staggering, wide-based gait in which the patient appears to be “drunk.” It is important to realize these tests may not be possible to perform in younger children who may not yet have highly developed speech or motor skills and may instead present with a refusal to speak or walk.

An ingestion-focused history is important in this population, as toxic ingestion may mimic concerning pathology. Caretakers should be asked about any medications both they and the patient may have been taking. Be sure to ask specifically if anyone who had been caring for the child suffers from anxiety or seizures, as they may respectively indicate access to benzodiazepines or AEDs.

The birth history, other than usual questions surrounding pregnancy, perinatal, and neonatal events, should focus on whether the child has had newborn screening for common metabolic disorders. Ideally, these records would be available for review but if they are not, one should never assume the results to be normal. Parents should be asked about any history of spontaneous abortions or if any siblings had abnormal results on their newborn screen. Although metabolic disorders associated with ataxia tend to manifest gradually, the presentation is often “unmasked” by the onset of systemic illness or a discontinuation in their daily vitamins.

**Physical and neurological examination**

The initial examination should focus on signs of systemic illness, including an assessment of vital signs and an examination of the skin for rash. Vital signs should be assessed for abnormal temperature to assess for infection. The triad of hypertension, bradycardia, and hypopnea may occur with increased intracranial pressure and has been shown to occur with ischemia arising from the posterior circulation.

A careful examination of the eyes is critical. Fundoscopic examination should be performed to assess for signs of increased intracranial pressure, whereas retinal hemorrhaging signals a high likelihood of nonaccidental trauma. Unilateral pupillary dilation can be the harbinger of temporal lobe herniation requiring immediate decompression. Bilateral nystagmus is often seen with toxic ingestion, whereas unilateral nystagmus implies a lateralizing defect and is therefore an indication for imaging. Any ophthalmoplegia can result from a lesion in the corresponding cranial nerve or their nuclei in the brainstem, an assessment of hearing and corneal sensation will help differentiate between the two possibilities. Sudden onset ocular findings, such as nystagmus or ophthalmoplegia, should be considered warning signs of posterior circulation stroke and warrant immediate imaging.

An important aspect of the physical examination in these cases is deciding whether the ataxia is because of cerebellar dysfunction. Speech can be affected in lesions of the cerebellum ipsilateral to the dominant hand and is commonly described as a “scanning speech” in which patients must carefully articulate individually spoken syllables. Finger-to-nose and heel-to-shin can be used to detect dysmetria, a sign indicating ipsilateral cerebellar damage. Reflex testing of the knees may demonstrate a “pendular” response, in which the leg swings more than four times after the tendon is struck. Finally, gait testing may reveal a staggering, wide-based gait in which the patient appears to be “drunk.” It is important to realize these tests may not be possible to perform in younger children who may not yet have highly developed speech or motor skills and may instead present with a refusal to speak or walk.

An assessment of the child’s mental status is critical part of the neurological examination for these patients. For many emergency department visits, the chief complaint may often be a change in behavior or personality, with ataxia revealed as a major feature only after taking the history or performing the physical examination. A formal assessment of the mental status should include the level of alertness, attention span, speech and language, and short-term memory. As we have discussed, an altered mental status is often the harbinger of urgent intracranial pathology such as ADEM, cerebellitis with mass effect, or stroke. Conversely, normal mentation is not normally seen with ingestion of many toxic substances such as AEDs or benzodiazepines. A patient with ataxia and an altered mental status should be assumed to have intracranial pathology until proven otherwise by MRI or unless there is an unequivocal history of toxic ingestion.

**Laboratory testing**

The utility of obtaining a complete blood count and a comprehensive metabolic profile has not been explicitly studied in acute ataxia; however, these tests should be ordered as a first pass screening tool—any derangement in electrolytes (with attention to magnesium and phosphate) should be corrected accordingly and subsequently invoke diagnostic algorithms themselves. Transaminitis may hint toward an inborn error in metabolism. Vitamins B1, B12, and E may be implicated in ataxia and should be evaluated in a patient with a history of poor nutrition or certain restrictive diets—these tests may be deferred until after admission.

Any suspicion of underlying metabolic disorder as suggested by a positive family history or obstetric history of spontaneous abortion, parental consanguinity, or that of failure or delay in achieving milestones preceding the onset of ataxia should be preliminarily investigated by obtaining metabolic screening laboratories: ammonia, lactate can screen for mitochondrial disorders such as Leigh syndrome, pyruvate dehydrogenase deficiency, or errors in catabolism. Abnormalities in these values or a suspicion for
such a disorder may invoke follow-up levels of pyruvate, urinary amino acids, organic acids, carnitine, and an acylcarnitine profile. However, these tests are better sent after admission and are best interpreted under the guidance of a geneticist or specialist in metabolic disorders.6

Imaging

The diagnostic yield of neuroimaging in children with acute ataxia has previously been estimated to be low, estimated by Whelan et al.3 in their review article to be approximately 2.5% for CT and 5% for MRI. However, the data they compiled were largely from older retrospective studies published from 1994 to, most recently, 2006.7,8,18,20 Since then there have been advances in the diagnostic capability of MRI that have allowed for a greater ability to resolve subtle areas of demyelination142,143 and cytotoxic edema.144 Advances in angiography and the use of contrast have also improved the ability to detect tissue edema and neoplasms.144

Rudloe et al. reported clinically urgent neuroimaging findings in 42 (12.5%) of 335 patients presenting with ataxia for less than seven days. Twenty-two of these patients had a tumor, and the remaining 20 had ADEM (12), infarct (three), encephalitis (one), transverse myelitis (one), hemorrhage (one), syringomyelia with hydrocephalus (one), and mastoiditis with epidermal abscess (one). CT was read as normal in 10 (26%) of 38 patients that subsequently showed pathology on MRI. Of 273 patients with symptoms for less than three days, 19 (7.0%) had significant imaging findings.9 Although Thakkar et al.10 did not explicitly report the total rate of positive imaging results, they did report eight (6.7%) of 120 patients as having been diagnosed with imaging-dependent diagnoses: cerebellitis (three), cerebellar stroke (two), ADEM (two), and cerebral vein thrombosis (one). The diagnostic yield of imaging cannot truly be assessed in the absence of prospective research.

MRI is superior to CT in detecting intracranial pathology. Inflammatory diseases of the brain are unlikely to be detected by CT. Rudloe et al.9 showed that of 10 patients diagnosed with ADEM, only two had lesions detected with CT, and the only patient with transverse myelitis had a normal CT. Transverse myelitis can only be detected with MRI and confirmed cases should be followed up with imaging of the optic nerves to evaluate for neuritis optica.145

CT is useful for quickly evaluating acute stroke and determining if it is hemorrhagic or ischemic; however, MRI may be superior in detecting small or very acute hemorrhagic lesions.29 Imaging of the posterior fossa with CT is further limited by beam hardening artifacts from surrounding bony structures.30 Although a study directly comparing CT with MRI in imaging the posterior fossa has not been done, Rudloe et al.9 demonstrated four children with cerebrovascular lesions in the posterior fossa, one of which was not detected with CT.

Imaging the brain with cranial CT may be critical in its rapid evaluation for neurosurgical issues such as the evolution of hemorrhage, mass effect, or obstruction of cerebral CSF outflow. In centers where rapid MRI is available, bypassing CT may save time, avoid unnecessary radiation and save resources as negative CT findings will not necessarily rule out clinically urgent pathology.146 On the other hand, rapid MRI as previously discussed has only been validated for assessing ventriculoperitoneal shunt malfunction and not for emergent headaches, depression in mental status, of focal neurological findings in the emergency department.65,105,106

Lumbar puncture

Abnormalities in the CSF, namely pleocytosis, are not unusual in the postinfectious ataxia disorders, APCA and cerebellitis.7,8,19,20 Cerebellitis is inconsistently associated with pleocytosis and cases with positive bacterial cultures are very rare.27,28 Protein levels may be increased in patients with GBS and MFS, but the sensitivity is 44% and 27%, respectively, during the first week of presentation.44 Although increased protein levels in the setting of normal cell counts can help confirm the diagnosis, a presumptive diagnosis of the peripheral neuropathies is largely clinical and has little dependence on LP.44,55 CSF protein levels are mostly important for prognosticating GBS and monitoring disease progression,44 and therefore can be reserved until after admission to an inpatient unit.

Large studies on the presenting signs of meningitis focus on fever, changes in mental status, hemorrhagic rash, and septic features to heighten the urgency of performing an LP.113,114,147 However, there is no evidence that ataxia with or without the presence of these features is more or less suggestive of bacterial meningitis. LP has been reported to precipitate brain herniation in patients with bacterial meningitis, and although CT may be helpful in finding contraindications to LP, a normal CT scan does not preclude the risk of herniation, which is best assessed clinically (papillary changes, irregular breathing, and so forth).148

LP can be diagnostic in the setting of subarachnoid hemorrhage, especially several days into the presentation as the sensitivity of CT drops over time.149,150 However, this phenomenon is exceedingly rare in children, and no such patients have presented with acute ataxia.9

The utility of obtaining CSF studies in the emergency department when directing both diagnosis and management of acute ataxia is uncertain and remains largely unstudied.

Toxicology screening

Toxic causes of ataxia can generally be identified from the clinical evaluation. Although the history is not always afforded by caregivers, questioning on specific substances or family members taking specific medications can be useful. Gieron-Korthals et al.7 reported an a priori history of ingestion in 61% of patients with positive toxicologic findings.

Screening for substances has long been considered an important test in the evaluation of acute ataxia,41 especially because many cases of ingestion will not necessarily present with a history of ingestion. Benzodiazepines remain a frequently ingested class of drugs, especially in toddlers and young children, that are known to cause ataxia. Broad screening will also help in detecting cases of cannabinoid ingestions, which may become more frequent in the face of liberalizing laws against the sale of marijuana and edibles.
Ethanol levels should be obtained as part of standard toxicology panels, even in young children. Urine or blood testing should be considered routine in cases where the patient is demonstrating decreased level of consciousness, acute confusional state, new onset of psychiatric symptoms, or a panic attack.\(^\text{151}\) As rapid confirmation of a toxic ingestion will help to exclude more serious intracranial pathology from the differential, AEDs known to cause ataxia are less commonly prescribed as they were at the time Gieron-Korthals et al. published their study of ataxia, with ingestions of these substances also less frequently reported.

**Conclusions**

The evaluation of a child with acute ataxia in the emergency department is a challenge for the clinician in determining the extent and timing of initial screening tests. In most studies, abnormalities detected by screening tests were nondiagnostic except for in a minority of patients. Therefore, careful analysis of the medical history should be carried out as the differential is broad, including central and peripheral causes of which some are life threatening. The spectrum of the etiologic factors in acute ataxia appears to have changed in the years since Gieron-Korthals et al. published their landmark article in 1994. Some of the major implicated changes are the use of new AEDs instead of phenytoin and carbamazepine and the use of new vaccines that may have reduced the incidence of classically post-varicellar cerebellar ataxia. Prospective data are needed to determine the relative incidence of different causes of acute ataxia.

From the evaluations that could be performed in the emergency room, toxicology screening should be considered in all children presenting with acute ataxia as it could be positive up to 49% of the cases or higher if the potential substance is known. Brain MRI is preferred over cranial CT when structural lesions are suspected because it offers a more complete evaluation of the posterior fossa. Head CT should be avoided to prevent radiation unless time is of the essence, as such is the case with hemorrhage, vascular disorders, hydrocephalus, or impending herniation. Imaging can be deferred for observation and follow-up in the clinically improving child who is otherwise well appearing. LP should be considered in patients with fever, meningeal findings, or an abnormal or declining mental status, but otherwise may be deferred until after admission. Other evaluations for less common causes should be considered in the context of the presenting symptoms, but evaluation in the ER is unlikely to change management. Urine catecholamines in a child with OMS will not be reported until the patient is already admitted and if it is negative will not rule out this disorder. There is insufficient evidence at the present time to establish a role for other tests in less frequent conditions such as autoantibody testing or searching for inborn errors of metabolism in children presenting with acute ataxia. Testing for metabolites—lactate, pyruvate, ammonia, amino acids, organic acids, carnitine, and acylcarnitine profile—should be done if there is any history of developmental regression or a family history of early deaths or pregnancy losses. Some tests could be normal in the first few days of a disease process, as is the case with CSF protein in GBS—a high index of suspicion is required in the appropriate clinical context.

Some institutions have protocols for the management of acute ataxia in the emergency department and practitioners should be familiar with these, but more research is needed to answer several fundamental questions with regards to the initial evaluation. Acute ataxia is a relatively common presentation in children seen by pediatric acute services and child neurologists as a whole, but the frequency of their specific etiologies might be low. We are in need of multi-center prospective research that is well enough powered to understand the rates of different causes and how to reliably test for them. Although a primary concern on initial assessment is to exclude serious causes of this clinical syndrome, one must also be able to quickly establish a diagnosis that might require rapid intervention. A good clinician should be able to keep an open mind when recognizing the essentially benign nature of acute ataxia in most children. The more confidence we have in evaluating these patients, the better we can provide guidance and reassurance to the families who may fear the worst.

**References**


