Clinical Reasoning: An 8-Year-Old With Acute Onset Ataxia

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Abstract

Acute ataxia is a common neurologic presentation in the pediatric population that carries a broad differential diagnosis. The tempo of the presentation, distribution of the ataxia (focal or diffuse), examination findings, and paraclinical testing may be helpful in guiding diagnosis and management. Although Guillain-Barré syndrome (GBS) and its variant, Miller Fisher syndrome (MFS), are well defined, frequently encountered acute autoimmune neuropathies, the GBS/MFS spectrum have at least 12 different phenotypes with distinct neurologic features, 4 of which include ataxia. These lesser-known variants can be diagnosed clinically, in the absence of conclusive laboratory or neuroimaging data, and should always be considered in an acute presentation of ataxia. In this article, we present a previously healthy 8-year-old with acute onset ataxia with associated hyporeflexia that occurred after resolution of a presumed viral infection. We discuss our approach to ataxia, the patient's neurodiagnostic odyssey, and highlight the final diagnosis of acute ataxic neuropathy without ophthalmoplegia—a rare incomplete MFS subtype. Owing to timely recognition of the condition, the patient was treated appropriately and recovered fully.

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Section 1

An 8-year-old, fully vaccinated, previously healthy right-handed boy presented with acute onset ataxia. Approximately 1 week before presentation, the patient developed a low-grade fever with accompanying headache. He improved clinically over the next several days. On the day of presentation, he awoke with an inability to walk. In the emergency department, he was afebrile but appeared fatigued. There was full range of neck motion. Speech and cognition were unimpaired. Visual acuity was 20/20, and extraocular movements were full without interruption. Strength was grossly full. There were no clear changes on light touch, pinprick, vibratory, temperature, or joint position sense testing. He had trace deep tendon reflexes in bilateral lower extremities, with preserved upper extremity reflexes. There was bilateral clumsiness of light bulb screwing motion with impaired finger-to-nose and heel-to-shin testing. Finger-to-nose testing revealed an oscillatory tremor because the target was approached. Finger tapping revealed sticky hands with thumb crease missed bilaterally. There was lack of coordination on rapid palmar-dorsal-hand-flip bilaterally. With eyes closed and arms extended, there were dance-like finger movements in both hands. While sitting or standing unsupported, there was frequent unidirectional lurching. Independent ambulation failed. With support, gait was wide-based. The patient fell when standing with his eyes closed, unsupported. Nausea and occasional emesis were elicited with movement.

Questions for Consideration:

1. What is the localization of this patient's presentation?

GO TO SECTION 2

Section 2

This patient presented with several distinct abnormal examination findings suggestive of a seemingly multifocal process. However, understanding the neuroanatomy of ataxia (impaired coordination of voluntary muscle movement) including the cerebellum, its afferents, and their correlation with coordination tasks can help with localization in this case.[1,2]

The cerebellum is anatomically divided into the cerebellar hemispheres and the midline cerebellum. The cerebellar hemispheres help integrate sensory input and motor planning for the coordination of complex tasks. Lesions may result in (ipsilateral) limb ataxia, dysdiadochokinesia, dysmetria, intention tremor, and scanning speech. The midline cerebellar structures are important in motor execution, rapid and slow eye movements, balance, lower extremity coordination, and vestibular function. Lesions may result in gait ataxia and imbalance, truncal ataxia, dysmetria, nystagmus and other ocular findings, titubation, and vertigo. Meanwhile, afferents from the brainstem and spinal cord through the inferior and middle cerebellar peduncles provide sensory, vestibular, visual, and proprioceptive input to the cerebellum. Damage to the brainstem can result in ataxia associated with cranial neuropathies. Disruption to the dorsal column, spinocerebellar tracts, and/or to the peripheral sensory and visual system can result in a sensory ataxia. Disruption of the vestibular system may result in disequilibrium, tinnitus, hearing impairment, and nystagmus.

The patient in this case had a wide-based unsteady gait (truncal/gait ataxia), errors of extremity trajectory and placement (dysmetria/intention tremor), and errors in motor sequence and rhythm tasks (dysdiadochokinesia). With visual input removed, his imbalance while standing (positive Romberg) and finger movements (pseudoathetosis) indicated a sensory ataxia. The nausea and emesis with movement supported a vestibular disequilibrium. Together, these signs/symptoms were consistent with central and peripheral nervous system pathology, suggesting direct cerebellar dysfunction as well as impaired vestibular, sensory, and proprioceptive afferent inputs. Not to be dismissed, the patient also had bilateral lower extremity hyporeflexia, indicative of a disruption somewhere along the lumbosacral reflex arc.

Over the next 2 days, while awaiting additional diagnostics, the patient's ataxia and disequilibrium worsened. He developed urinary retention, poor orientation, and inconsistent performance of simple commands.

Questions for Consideration:

1. What is the differential diagnoses for this presentation?
2. What diagnostics would you perform?

GO TO SECTION 3

Section 3

In the differential for ataxia, one must place emphasis on tempo of the disease course, distinguishing between acute, subacute, or chronic *and* the distribution of the ataxia (focal vs diffuse).[3] This patient's presentation was decidedly acute and diffuse. The differential diagnosis for an acute, diffuse ataxia includes toxic ingestion (e.g., alcohol, phenytoin, carbamazepine, phenobarbital, benzodiazepines, antihistamines, lithium, toluene, and chemotherapeutics), acute cerebellar ataxia (ACA), opsoclonus myoclonus ataxia syndrome (OMAS), brainstem encephalitis, Guillain-Barré syndrome (GBS) variants, demyelinating conditions (e.g., acute disseminated encephalomyelitis/multiple sclerosis), vascular etiologies (stroke, dissection), neoplasm, lupus (SLE), concussion, and complex migraine/psychogenic causes as diagnoses of exclusion.

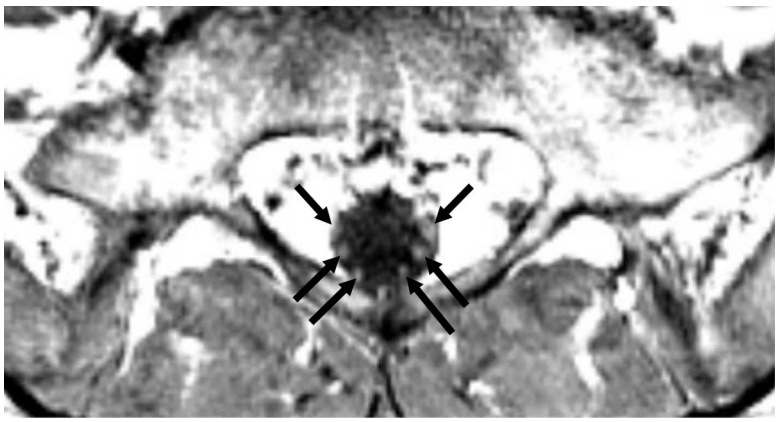
A thorough history of no prior accidental ingestion or head strike argued against a toxidrome and concussion. A lack of supporting systemic symptoms left lupus unlikely. An acute presentation of multifocal neoplasm involving the posterior fossa and the lumbosacral spine would be extremely rare. Stroke involving the vertebrobasilar territory and lumbosacral spinal arteries would be mechanistically unlikely. OMAS was considered, even without opsoclonus, because ataxia can be the heralding sign[4,5]; however, his older age and rapid onset made OMAS less plausible. Brainstem encephalitis was considered given his ataxia, encephalopathy, and nausea; however, in addition to the lumbosacral findings, the lack of meningismus, seizure, cranial neuropathies, autonomic instability, or bulbar dysfunction made this less likely. Similarly, ACA was a consideration given the patient's postinfectious explosive ataxia with encephalopathy; however, the hyporeflexia and urinary retention did not fit clinically. A demyelinating syndrome was discussed, given the postinfectious patchy CNS involvement, but it was believed to be unusual in this distribution. Highest on the differential were the GBS variants, given the constellation of acute ataxia, hyporeflexia, urinary retention, and encephalopathy, but the absence of weakness and ophthalmoplegia were initially puzzling.

To help distinguish between this broad differential, multimodal diagnostics were performed including serum, urine, and CSF testing for toxic, infectious, and paraneoplastic etiologies, complete neuroaxis MRI with and without contrast, and whole-body PET. MRI revealed postcontrast lumbosacral enhancement consistent with radiculitis, without intracranial pathology (Figure). PET scan was negative. CSF yielded a lymphocytic pleocytosis and normal protein. Gram stain and cultures were negative. All remaining laboratory results were unrevealing or pending at the time of therapeutic initiation.

Questions for Consideration:

1. Does this newly acquired information help narrow down your differential?
2. What therapies would you initiate?

Figure Lumbar Spine MRI Findings Consistent With Radiculitis



Contrast-enhanced T1-weighted axial image shows mild diffuse thickening and enhancement of the cauda equina nerve roots bilaterally (arrows).

GO TO SECTION 4

Section 4

The negative PET and urine catecholamines eliminated OMAS. Lupus laboratory results were negative. The lumbosacral radiculitis without intracranial or spinal pathology on MRI eliminated tumor, demyelinating disease, and stroke. MRI-negative brainstem encephalitis, GBS, and acute cerebellar ataxia are not uncommon[3,4]; therefore, these conditions remained on the differential. The lymphocytic pleocytosis with normal CSF protein indicated a postinfectious or parainfectious inflammatory process. As such, broad infectious coverage was initiated with antibiotics and antivirals. Simultaneously, IV immunoglobulin (IVIG) therapy was run over 5 days to treat for GBS variants. Antiemetics were given for nausea. Infectious coverage was peeled back with the return of negative CSF studies. The patient's symptoms dramatically improved over his 13-day hospitalization. At discharge, he transitioned to oral medication, voided without catheterization, ambulated independently, and returned to baseline cognition. After the remainder of his outstanding laboratory results resulted negative, the patient was diagnosed with acute ataxic neuropathy (without ophthalmoplegia) (AAN), a GBS subtype.

Discussion

GBS is a broad term used to describe a spectrum of related acute autoimmune neuropathies. In 2014, The GBS Classification Group proposed diagnostic criteria based on an inclusive set of clinical features to differentiate each disease phenotype on the GBS spectrum, primarily designed to help clinicians make a diagnosis without reliance on paraclinical testing[6] (Table). AAN is an incomplete Miller Fisher syndrome (MFS) subtype of GBS. It is a large fiber sensory neuropathy characterized by ataxia without weakness, hypersomnolence, or ophthalmoplegia; however, the abovementioned authors describe a complicated interplay of central and peripheral nervous system dysfunction. They also acknowledge imperfections in their classification system because the variants exist on a spectrum with pathology that has not yet been fully elucidated. Although encephalopathy is not classically associated with AAN, the remainder of the patient's symptoms were consistent with this variant and the cognitive disturbances did not meet the threshold of hypersomnolence seen in Bickerstaff brainstem encephalitis; therefore, AAN seemed the most appropriate diagnosis.

CSF analysis, nerve conduction studies, and antiganglioside antibody testing may be helpful in supporting the diagnosis, but studies from adult patients suggest they are often inconclusive early in the diagnostic odyssey and may differ in frequency from classic MFS. Anti-GQ1b and/or anti-GD1b antibodies are undetectable in ~50% of AAN cases.[7] Many patients with GBS variants will have absent CSF albuminocytologic dissociation, particularly within the first week of symptom onset.[7-9] Similarly, performance of nerve conduction studies within the first week of symptoms may not fulfill criteria for a specific electrophysiologic subtype of neuropathy.[7,10] In a small cohort of 11 heterogenous pediatric patients with MFS variants (including AAN), the results suggest potentially higher frequency of unilateral involvement of ophthalmoplegia, ataxia, and autonomic symptoms, less anti-GQ1b positivity, and areflexia, with similar disease course and recovery, as compared with their adult counterparts.[11] Ultimately, a firm clinical suspicion should not delay treatment with appropriate immunotherapy. IVIG at a dose of

Table Clinical Phenotypes of GBS, MFS, and Their Subtypes as Proposed by the 2014 GBS Classification Group[6]

Category	Subtype	Pattern of weakness	Ataxia	Hypersomnolence
GBS	Classic GBS	Four limbs	+/−	−
	Pharyngeal-cervical-brachial weakness	Bulbar, cervical, and upper limbs	−	−
	Acute pharyngeal weakness	Bulbar	−	−
	Paraparetic GBS	Lower limbs	−	−
	Bifacial weakness with paresthesias	Facial	−	−
MFS	Classic MFS	Ophthalmoplegia	+	−
	Acute ophthalmoparesis	Ophthalmoplegia	−	−
	Acute ataxic neuropathy	No weakness	+	−
	Acute ptosis	Ptosis	−	−
	Acute mydriasis	Paralytic mydriasis	−	−
	BBE	Ophthalmoplegia	+	+
	Acute ataxic hypersomnolence (incomplete BBE)	No weakness	+	+

Abbreviations: BBE = Bickerstaff brainstem encephalitis; GBS = Guillain-Barré syndrome; MFS = Miller Fisher syndrome.

2 g/kg given over 5 days remains the standard of care for GBS. In addition, with the absence of positive paraclinical data, and significant clinical overlap between other conditions with ataxia, broad spectrum treatment may be warranted, such as in our case.

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John Robert McLaren, MD	Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design
Matthew Kyler Mitchell	Harvard Medical School, Boston, MA	Drafting/revision of the manuscript for content, including medical writing for content
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Kevin Joseph Staley, MD	Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston	Drafting/revision of the manuscript for content, including medical writing for content

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