

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Ataxia

**Variant 1:** Slowly progressive ataxia, or ataxia of long duration (adult or child).

Radiologic Procedure	Rating	Comments	RRL*
MRI head without and with contrast	8		None
MRI head without contrast	7		None
MRI cervical thoracic and lumbar spine without and with contrast	7	Ataxia can be of spinal origin. Consider if brain imaging is negative or inconclusive.	None
MRI cervical thoracic and lumbar spine without contrast	6	Ataxia can be of spinal origin. Consider if brain imaging is negative or inconclusive.	None
CT head	5		Low
FDG-PET head	3		High
MRI spectroscopy head	2		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 2:** Acute ataxia (< 3 hours) as a manifestation of suspected stroke (adult or child).  
(Also see the ACR Appropriateness Criteria® topic for cerebrovascular disease).

Radiologic Procedure	Rating	Comments	RRL*
MRI head with or without contrast	8	MR preferred if treatment is not unreasonably delayed. Combined vascular and cerebral evaluation should be considered. Fat saturated T1 axial images.	None
MRA head and neck	8	MR preferred if treatment is not unreasonably delayed. Combined vascular and cerebral evaluation should be considered.	None
CTA head and neck	8	MR preferred if treatment is not unreasonably delayed. Combined vascular and cerebral evaluation should be considered.	Low
CT head	8	CT perfusion is less accurate in the posterior fossa. MR preferred if treatment is not unreasonably delayed. Combined vascular and cerebral evaluation should be considered.	Low
MRI cervical spine without and with contrast	5	Fat saturated T1 axial images.	None
MRI cervical spine without contrast	4		None
MRI spectroscopy head	2		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

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**Clinical Condition:** Ataxia

**Variant 3:** Acute or subacute ataxia as a manifestation of suspected infection (adult or child).

Radiologic Procedure	Rating	Comments	RRL*
MRI head without and with contrast	8		None
MRI head without contrast	7		None
MRI cervical spine without and with contrast	6	Ataxia can be of spinal origin. Consider if brain imaging is negative or inconclusive.	None
MRI spectroscopy head	6	May help distinguish abscess from other masses.	None
MRI cervical spine without contrast	5	Ataxia can be of spinal origin. Consider if brain imaging is negative or inconclusive.	None
MRA head without and with contrast	5		None
CTA head	5		Low
CT head without and with contrast	5		Low
CT temporal bone	5	Useful when skull-based or middle ear disease suspected.	Low
MRA head without contrast	4		None
CT head without contrast	4		Low
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 4:** Acute ataxia following head trauma, less than 24 hours (adult or child).

Radiologic Procedure	Rating	Comments	RRL*
CT head without contrast	9		Low
MRI head without contrast	8		None
CT temporal bone	7	Useful when skull-based or middle ear disease suspected.	Low
MRI head without and with contrast	7		None
MRI neck without and with contrast	6		None
CT head without and with contrast	6		Low
CTA head and neck	6		Low
MRA head and neck	6		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

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# ATAXIA

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## Summary of Literature Review

Ataxia is a term that is used to describe abnormality in the coordination of movement. Manifestations commonly include a wide-based unsteady gait and poor coordination of the extremities. There can be associated abnormality in ocular motility and poor coordination of speech. Each of these alterations can relate to abnormal motor trajectory or placement during active movement (dysmetria), and/or to errors in the sequence and speed of motor activity. Abnormality in the rate, force, direction, and/or path of movement results in movement that is imprecise and dysfunctional. Purposeful, rapid alternating motion rates of muscle groups become slower and less fluid (dysdiadochokinesis), and the motion may have diminished rhythm (dysrhythmokinesis) [1]. Early in the course of an ataxia-causing disease process there may be decreased resistance to passive movement (hypotonia), and muscle stretch reflexes (DTRs) may demonstrate a “pendular” response. Intention tremor may be present when initiating or performing an activity, especially when the ataxia is of cerebellar origin. Ocular nystagmus, skew deviation, disconjugate saccades, and altered ocular pursuit movements can also be seen as a component of ataxia. As an anatomic localizing sign, a wide-based stance, with feet several inches apart, is the most common, but not specific, clinical sign of cerebellar disease. Truncal instability and rhythmic tremor of the body or head (titubation) occur especially, but not exclusively, in association with disorders that involve the cerebellar midline. Physical findings associated with ataxia, and the utility of these findings relative to anatomic localization have been reviewed [1,2].

Ataxia can separately arise from disorders that involve the cerebellum, spinal cord, brainstem, vestibular nuclei, thalamic nuclei, white matter tracts of the brain stem and cerebral hemispheres, cerebral cortex (especially the frontal lobes), and peripheral sensory nerves. Because the anatomic regions responsible for ataxia are multiple, an effective imaging evaluation is often complex. Additionally, in patients with distinct clinical ataxia, appropriate magnetic resonance imaging (MRI) or computed tomography (CT) imaging of the cerebellum itself, or of the entire brain and spinal cord, may be entirely normal. This is most likely to occur early in the course of toxic, metabolic, or other progressive disorders associated with ataxia.

The medical disorders that cause ataxia are numerous and complex, and they are often individually quite uncommon. The development of prospective generalized recommendations for imaging, for the inclusion of anatomic regions to be studied, and for the use of specific protocols or pulse sequences is therefore imprecise. The purpose of this discussion, and of the guidelines presented below, is to categorize the diverse disorders that may present with ataxia and to suggest general imaging guidelines that may be useful for patients with the most common clinical presentations and underlying disorders. For individual patients, study design will be significantly compromised if the history that accompanies the patient is not precise or sufficient relative to the clinical and family history, to specific physical findings and/or to the results of relevant laboratory studies, many of which are quite complex.

Ataxia-associated disorders have been the subject of several classification schemes [3,4]. For basic clinical and imaging purposes, however, these disorders can be approached on the basis of age at onset, potential disease mechanism, and anticipated clinical urgency for excluding a disorder that requires immediate diagnosis and management. Disorders associated with vertigo, the subjective illusion of movement, can be associated with apparent incoordination. Vertigo is a separate ACR Appropriateness Criteria<sup>®</sup> topic and will not be readdressed here [5].

## Classification of Disorders Causing Ataxia

### *Mass Lesions*

The exclusion of a posterior fossa mass lesion is often an important consideration in evaluating a patient with ataxia. The suspected mass can be primary or metastatic, and it can be intra-axial or extra-axial in location. In pediatric patients the most common intra-axial posterior fossa lesions are medulloblastoma, cystic astrocytoma, ependymoma, and brain stem glioma. In adults, intra-axial hemangioblastomas, choroid plexus papillomas,

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extra-axial meningiomas, and a host of intra-axial, extra-axial, or diffuse leptomeningeal metastatic processes become more prevalent. Isolated frontal lobe and thalamic mass lesions can also present with varying manifestations of gait and limb ataxia. Unless there is a contraindication, MRI, without and with contrast, is almost always superior to CT for the initial exclusion and characterization of a posterior fossa or other intracranial mass lesion.

Lhermitte-Duclos disease (dysplastic gangliocytoma) is a slowly growing benign cerebellar hamartoma or congenital malformation [6]. Symptoms correlate with local mass effect. MRI demonstrates a cerebellar hemisphere mass that involves the cortex and folia and is generally of increased T2 signal intensity. There are also characteristic internal curvilinear bands that are isointense with cerebellar cortex [6-8]. The mass does not enhance with contrast, and it may demonstrate restricted diffusion [6-8]. Cowden syndrome, an autosomal dominant disorder characterized by cutaneous and noncutaneous hamartomas and by breast, thyroid, gastrointestinal and urologic gastric ulcer and GU neoplasias, is frequently associated [6,7].

Paraneoplastic cerebellar degeneration is clinically characterized by the subacute or acute onset of gait and limb ataxia, dysarthria, and ocular dysmetria [9]. It can occur in association with essentially any tumor type but most commonly occurs with breast, gynecologic, and lung tumors, and in association with Hodgkin's disease [9]. Tumor seeding of brain parenchyma is not demonstrated with tissue sampling or with imaging. Several antineuronal antibodies have been identified in serum and in tissue, depending on the originating tumor cell type. MRI is generally normal until late stages of the disorder when mild to moderate cerebellar cortical atrophy becomes evident [9]. Uncommonly there can be increased T2 signal intensity in the cerebellum or in other simultaneously involved brain parenchymal areas [10]. CT imaging and/or positron emission tomography (PET) imaging are indicated when an underlying primary is not evident [11].

#### *Vascular Disorders*

Strategically located ischemic or hemorrhagic insults can result in distinct and often prominent ataxia. Ataxia-associated infarction can be isolated to vascular distributions within portions of the cerebellum, medulla, pons, mesencephalon, red nucleus, thalamic nuclei, posterior limb of the internal capsule, or to the frontal or parietal cerebral cortex [12-18]. Medially positioned infarctions involving the pons and medulla are uncommonly associated with ataxia [14,15]. Several named syndromes are associated with ataxia and focal regions of brainstem infarction [18,19]. Infarction in the distribution of the posterior inferior cerebellar artery (lateral medullary syndrome or Wallenberg syndrome) is

the most common pattern of brainstem infarction that is associated with a specific syndrome of ataxia. Symptoms include ipsilateral hemiataxia, vertigo, dysarthria, ptosis, and miosis. While brainstem and cerebellar infarctions are predominately arterial in origin, venous infarction should also be considered [20]. The radiologic evaluation of ataxia generally requires MRI, with water diffusion characterization and with time-of-flight MR angiography. Use is also made of neck vessel MRI, using T1-weighted images, without and with fat saturation, to exclude the possibility of dissection [21-23]. MR venography should be accomplished if there is consideration of central or dural venous thrombosis. Catheter-based diagnostic angiography and/or CT angiography (CTA) is occasionally necessary [23].

When the posterior fossa or supratentorial brain parenchyma is involved, vascular malformations, angiopathy, or aneurysm rupture can each lead to the acute development of ataxia. When there is consideration of acute or subacute hemorrhage, CT imaging of the brain and CTA may replace or supplement MRI.

MRI is the definitive diagnostic procedure for characterizing superficial siderosis [24]. In this disorder hemosiderin accumulates in subpial layers of brain and spinal cord as the result of recurrent, often silent, subarachnoid hemorrhage. The most prominent symptoms are slowly progressive ataxia and hearing loss. [24] With MRI there is low superficial T2 signal intensity over cortex, brain stem, and/or spinal cord with usual cerebellar atrophy.

#### *Infectious and Postinfectious Processes*

A number of infectious and postinfectious processes can be responsible for the development of ataxia. To detect infectious-process-related alterations in the cerebellum, MRI without and with contrast administration, provides a distinct advantage over CT. This advantage is due to superior contrast resolution of MRI, and to the absence of CT-related artifacts that can occur in association with bone at the margins of the posterior fossa.

Bacterial cerebellitis can occur in association with meningitis or with cerebritis involving the cerebral hemispheres. It can also occur independently. Penetrating trauma or transdural extension of an epidural process, most commonly from the temporal bone, also needs to be considered. Diffusion imaging and MR spectroscopy can narrow the differential diagnosis [25,26]. Multiple viral processes, including herpes and arbovirus, can also be associated with brainstem or cerebellar involvement [27].

Variant Creutzfeldt-Jakob disease (vCJD), also known as bovine spongiform encephalopathy (BSE), familial Creutzfeldt-Jakob disease (fCJD), and sporadic Creutzfeldt-Jakob disease (sCJD) are the most common

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prion-associated spongiform encephalopathies. Both vCJD and sCJD present with behavioral, emotional, and intellectual deterioration, followed by development of ataxia and dysarthria. Progression is to stupor and coma, with associated myoclonus being prominent in sCJD. The clinical course is more prolonged in vCJD. MRI demonstrates increased T2 signal intensity, and increased signal intensity on inversion recovery and diffusion-weighted sequences, in the heads of the caudate nuclei, the putamen, and regions of frontal, parietal, and occipital cortex. These alterations in signal intensity can initially be asymmetric [28]. There is eventual diffuse volume loss. While all forms of CJD can have increased T2 signal intensity and restricted diffusion in the thalamic nuclei and in the pulvinar bilaterally, this focal alteration is especially prominent in vCJD [28].

Acute cerebellitis, also called acute cerebellar ataxia, is a para-infectious disorder that predominately, but not exclusively, occurs in childhood. Symptoms include headache, ataxia, photophobia, and varying findings associated with potential increased intracranial pressure or brainstem involvement. MRI demonstrates increased T2 signal intensity in the cerebellar hemispheres with associated mass effect [29]. Bilateral abnormality is more common than unilateral abnormality. There may be obstruction of cerebrospinal fluid (CSF) flow with enlargement of the lateral ventricles and upward herniation of posterior fossa structures [29]. There may also be cerebellar meningeal enhancement following contrast administration. Surgical decompression of the posterior fossa may be necessary [30]. Follow-up imaging may demonstrate cerebellar atrophy [31].

Bickerstaff encephalitis is a brainstem and cerebellar inflammatory disorder that most commonly follows a viral illness. It is characterized by ataxia and ophthalmoplegia, with MRI demonstrating mass effect, increased T2 signal intensity, and restricted diffusion within portions of the pons, medulla, and cerebellum [32,33].

Fisher syndrome, a variant of the Guillain-Barré syndrome, involves the peripheral and central nervous system. It is clinically characterized by ophthalmoplegia and cerebellar ataxia, and it is associated with transient high T2 signal intensity within the cerebellum and/or brainstem [34]. Enhancement of cranial nerves and spinal nerve roots can be demonstrated, and there may be increased T2 signal intensity within the posterior portions of the spinal cord [35,36]. FLAIR images often demonstrate this alteration to greatest advantage in the acute phase. Cerebellar atrophy is generally demonstrated during the convalescent phase.

### *Trauma*

Gait instability is a frequent component of concussion syndrome, and it may persist in association with a post-traumatic encephalopathy. Symptoms may be due to damage to the posterior fossa, vestibular, or brain stem structures. Persisting ataxia can also relate to frontal lobe injury [37]. One possible explanation for the association of ataxia with a frontal lobe lesion of any origin is interruption of the frontopontocerebellar tract (Arnold's bundle). This tract originates in Brodmann's area 10 and carries information regarding intentional movement to the contralateral cerebellum via the middle cerebellar peduncle [37]. Interruption of this tract along its course, or at its origin, deprives the cerebellum of frontal cortical input, resulting in impaired coordination and locomotion. In the presence of acute trauma, or in subjects with progressive post-traumatic ataxia, an expanding cyst or extra-axial hematoma should separately be considered.

### *Demyelinating Disorders*

Multiple sclerosis patients commonly present with or subsequently manifest persisting ataxia. In these patients, MRI (without and with contrast), diffusion imaging, spectroscopy, perfusion imaging, and magnetization transfer imaging can each support but not establish the diagnosis. The presence of multiple oval periventricular regions of increased T2 signal intensity, generalized cerebral volume loss, callosal and optic nerve involvement, and ring enhancement of active lesions is typical. MRI findings, and the utility of advanced MRI techniques for patient evaluation and management, have recently been reviewed [38].

### *Congenital Disorders*

A large number of ataxia-associated disorders occur on a congenital basis [4]. In each of these processes MRI is preferred to CT. All of these disorders will most commonly manifest ataxia during early childhood development. Some of them are sporadic, while others have a known or an apparent genetic basis [4]. Clinical abnormalities that occur in association with congenital ataxia can include mild to severe mental retardation, hearing loss, optic atrophy, cataract, growth retardation, seizures, cleft palate, and either spasticity or diminished muscle tone. In these well-characterized congenital ataxia-associated disorders, imaging findings generally include nonspecific hypoplasia of the cerebellar vermis, hypoplasia of the entire cerebellum, or congenital cerebellar developmental dysplasia. Additional associated imaging alterations can include brain stem hypoplasia, lissencephaly, aprosencephaly, microcephaly, or variable and less prominent cerebral developmental alteration.

Though the disorders that can present as congenital ataxia are individually uncommon, a small number are more frequently recognized [39,40]. Dandy Walker Syndrome, with ataxia, nystagmus, cranial nerve palsies, apneic episodes, hydrocephalus, and cognitive dysfunction, is

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characterized by hypoplasia of the cerebellar vermis with an associated CSF collection that is predominately posterior to the cerebellum but continuous with the fourth ventricle [39]. The torcula is usually elevated and the posterior fossa usually enlarged. Hydrocephalus is frequently associated, and there may be anomalies of cerebral development that involve the cerebral cortex and corpus callosum [39]. Differentiation from other congenital or acquired posterior fossa cysts is essential.

Joubert syndrome, with congenital ataxia, hypotonia, and oculomotor ataxia, has unique imaging alterations that involve the midbrain and cerebellum (“molar tooth” contour of brainstem or “bat wing” configuration of fourth ventricle) [41]. Four types have been identified, each with somewhat variable clinical and imaging features, and with genetic alterations that involve different loci [42].

Rhombencephalosynapsis is a rare cerebellar dysplastic process that can occur alone or in association with other developmental anomalies [40]. In rhombencephalosynapsis there is vermian agenesis with fusion of the cerebellar hemispheres, apposition or fusion of the dentate nuclei, and fusion of the superior cerebellar peduncles. There is usually enlargement of the lateral ventricles, and there may be fusion of the thalamic nuclei [40]. There is a wide spectrum of clinical symptomatology, and some patients are clinically normal [40].

Congenital ataxia can also occur in association with perinatal cerebral infarction and in association with congenital cytomegalovirus or other infectious processes of the central nervous system [39,43]. Though uncommon relative to other forms of cerebral palsy, the imaging correlates of ataxic cerebral palsy have not been well defined [44].

#### *Hereditary and Idiopathic Degenerative Processes*

The hereditary ataxias are classified on the basis of their causative gene (when known) and their pattern of inheritance (autosomal dominant, autosomal recessive, x-linked, or mitochondrial). In each of these disorders MRI is the preferred imaging modality. Among this group of patients, a broad range of potential diagnostic considerations is often suggested by family history, by findings on physical examination, and, in symptomatic patients, by MRI evidence of atrophy involving the cerebellum and varying combinations of the pons, medulla, spinal cord, cerebral cortex and optic nerves. Dentate calcification may also be identified on CT imaging. Definitive diagnosis, however, relies on molecular genetic testing. While cerebellar ataxia is the dominant and occasionally the only clinical finding, spasticity, neuropathy, seizures, extrapyramidal symptomatology, mental retardation, cognitive decline,

nystagmus, visual loss, spasmodic cough, and migraine-like episodes may also be associated.

Among the identified autosomal dominant spinocerebellar ataxias (AD-SCAs), specific diagnostic nomenclature is replacing less specific terms such as “spinocerebellar degeneration,” “Marie’s ataxia,” and olivopontocerebellar atrophy (OPCA). Among the AD-SCA disorders, 22 separate and distinct genetic abnormalities have now been identified. The term OPCA continues to be used only as a label for cases that have a clinical and pathology-related combination of “cerebellar-plus” symptomatology, have imaging correlates of cerebellar and brainstem atrophy, and have an (as yet) unidentified genetic basis [45]. The designation of “idiopathic late onset cerebellar ataxia” is separately used to describe a different and significantly large group of adult patients with predominant cerebellar symptomatology, absence of a family history, and absence of an identified genetic marker [46]. In these patients MRI generally demonstrates cerebellar and pontine volume loss [47].

SCA2 is one form of AD-SCA. It is caused by the presence of 32 or more CAG trinucleotide repeats on the ATXN2 gene. Symptoms include slowly progressive ataxia, dysarthria, nystagmus and initially brisk but later absent tendon reflexes, with associated peripheral neuropathy. Dystonia, Parkinsonism, and dementia may also be present in SCA2. Symptoms are more rapidly progressive when they have their onset before 20 years of age. Imaging findings include cerebellar and pontine volume loss and deep white matter alterations that may also involve the cerebral hemispheres. Although SCA2 is a relatively common form of AD-SCA (13% of AD-SCA cases in one study), clinical and imaging features do not allow a definitive diagnosis. Molecular genetic analysis is necessary. Many, but not all cases as Marie’s ataxia and AD-OPCA are thought to represent SCA2.

SCA3 (Machado-Joseph disease or MJD) accounts for 23% of patients with AD-SCA. Symptoms most commonly include an onset in the second to fourth decade of cerebellar ataxia, spasticity, peripheral neuropathy, bulbar dysfunction with facial and tongue atrophy, and occasional myoclonus or intellectual impairment. Subtypes have been described. MRI alterations include volume loss involving the cerebellum, pons and medulla, and a linear region of high T2 signal intensity along the posterior and medial margins of the globus pallidus.

Dentorubral-pallidolusian atrophy (DRPLA) is characterized by progressive ataxia, choreoathetosis, and dementia or character changes when the disorder occurs in adults. In children it is characterized by ataxia, myoclonus, epilepsy, and progressive intellectual deterioration. [48]. MRI demonstrates cerebellar and brainstem volume loss with cerebral cortical atrophy [49].

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Less frequently there is increased T2 signal intensity in deep white matter of the cerebral hemispheres, in the thalamus, and in the brainstem [49]. Diagnosis is established through the identification of >48 CAG repeats in the DRPLA gene [48].

Autosomal recessive hereditary ataxias can be associated with multiple underlying genetic disorders. Several are described below. The most common is Friedreich's ataxia. It has a population frequency of 1-2/50,000, and most commonly has its onset within the first or second decade. Symptoms are progressive and are characterized by ataxia, diminished muscle stretch reflexes, upgoing toes, sensory loss for vibration and position, pes cavus, and cardiomyopathy [50,51]. Imaging findings include diminished cross sectional area of the spinal cord and medulla, and inconsistently, the presence of volume loss involving the cerebellum [50,51]. Diagnosis is based on molecular genetic testing with GAA expansions in the FRDA gene, and other FRDA gene mutations [51].

Ataxia-telangiectasia (A-T) is an autosomal recessive hereditary ataxia with findings of progressive cerebellar ataxia, telangiectasias of the conjunctivae, oculomotor apraxia, choreoathetosis, and frequent infections. Symptoms begin between one and four years of age, and there is a population-based prevalence of 1/40,000-100,000. There is an increased risk for leukemia and lymphoma, in part relating to an increased sensitivity to ionizing radiation. MRI demonstrates initial selective atrophy of the lateral portions of the cerebellar hemispheres, with subsequent extension of volume loss to involve inferior and superior cerebellar cortical regions [52]. The vermis also becomes atrophic, more in its superior than in its inferior portions [52]. Laboratory testing supports the diagnosis of A-T by identifying elevated serum alpha-fetoprotein, the absence of ATM protein in blood mononuclear cells [53], the presence of a 7:14 chromosome translocation in peripheral lymphocytes, and the presence of immunodeficiency. Several less common AR-SCAs have also been identified, but will not be discussed here [3].

The fragile X tremor/ataxia syndrome (FXTAS) is an X-linked cause of progressive ataxia. Fragile X syndrome, a separate but related disorder, is the most common genetic cause of mental retardation [54]. It results from silencing of the x-chromosome, fragile-X mental retardation 1 (FMR1) gene by >200 CGG repeats at the 5'-UTR location on the x-chromosome [54]. Predominant clinical findings include a characteristic facies, developmental delay, and mental retardation [54].

FXTAS, however, involves adults, predominately males, who are *carriers* of the fragile-X syndrome [55]. All have "premutation" alleles that contain 55-200 CGG repeats within the FMR1 gene [56]. Significant and progressive

clinical findings include tremor, ataxia, autonomic instability, Parkinsonism, and cognitive decline [55,57]. Age at onset and severity have a positive correlation with CGG repeat length. Characteristic FXTAS brain MRI findings include brain stem atrophy and cerebral cortical atrophy. There is usually increased T2 signal intensity in the white matter of atrophic middle cerebellar peduncles, as well as in deep and in subependymal cerebral white matter [58].

Multiple system atrophy (MSA) is a sporadic neurodegenerative disorder that can initially be manifest by ataxia (MSAc) or by Parkinsonism (MSAp) [59,60]. Onset is generally after age 50, and early additional findings can include prominent autonomic dysfunction and spasticity. Previously reported cases of sporadic OPCA and Shy-Drager syndrome most likely represent what is now known as MSA. MSAc is characterized by gait and limb ataxia, by dysarthria, and by oculomotor abnormalities that initially are similar to the findings observed in late onset cerebellar ataxia. Dysautonomia and Parkinsonism will eventually develop [59]. MRI demonstrates atrophy of the pons, cerebellum, and putamen, and there may be increased T2 signal intensity in the pons and middle cerebellar peduncles. The putamen are generally low in signal intensity on T2 weighted images, though there is often a narrow band of increased T2 signal intensity at the lateral aspect of the putamen [59-61].

Progressive ataxia is occasionally associated with mitochondrial disorders such as MERRF (myoclonic epilepsy with ragged red fibers), NARP (neuropathy, ataxia, and retinitis pigmentosa), Leigh syndrome, and Kearns-Sayre syndrome [62]. Additional clinical manifestations such as seizures, deafness, diabetes mellitus, cardiomyopathy, retinopathy, and short stature are often associated. In NARP, cerebral and cerebellar atrophy may be noted on MRI. In Leigh syndrome, bilateral symmetric low attenuation may be present in the basal ganglia on CT, and increased T2 signal intensity may be seen in the brainstem and/or basal ganglia on MRI [63].

A deficiency of coenzyme Q10 has been described in individuals with cerebellar ataxia, usually with childhood onset and often associated with seizures [64]. MRI may demonstrate cerebellar volume loss [64]. Symptoms may respond to treatment with coenzyme Q10.

Vanishing white matter disease is an inherited early childhood leucoencephalopathy whose most prominent initial symptom is ataxia [65]. Onset most commonly occurs at 2 to 6 years of age, though adolescent and adult onset have been described. MRI demonstrates diffuse increased white matter T2 signal intensity and both a progressive and extensive loss in volume of cerebral and

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cerebellar white matter. Subcortical white matter may initially be spared [65].

#### *Paroxysmal Disorders*

Paroxysmal ataxia has been associated with several disorders, including epilepsy and migraine, as well as with a transient limb and trunk ataxia that can occur with high systemic fever in otherwise healthy children. These disorders can be idiopathic or can be associated with abnormalities in membrane calcium or potassium channel function, or with altered synaptic glutamate transport [66-68]. MRI may be normal, may demonstrate cerebellar volume loss, or may demonstrate extensive areas of cortical increased T2 signal intensity that may correlate with the possible simultaneous occurrence of hemiplegic migraine or recent seizure activity. MRI is the imaging modality of choice.

#### *Spinal Cord and Peripheral Nerve-Related Ataxia*

Ataxia that is potentially due to pathologic processes that originate within the spinal cord, or within the roots/nerves that originate from the spinal cord, requires high resolution T1 and T2-weighted axial and sagittal imaging without and with contrast that focuses on the posterior columns and on the nerve roots. Findings in pernicious anemia depend on the duration and severity of the disorder.

There may be early localized or relatively diffuse cord swelling with increased T2 signal intensity that is usually most evident in the posterior columns [69,70]. Late atrophy and persistent gliosis may develop, or all findings may resolve with treatment [69]. In the presence of hypertrophic, inflammatory, or postinfectious polyneuropathies, nerve root enhancement and enlargement may be demonstrated with MRI [36].

#### *Nutritional Deficiency, Toxins and Drugs*

In each of these disorders MRI is the preferred imaging modality. Solvent abuse or toxic exposure to solvents can result in gait impairment and in encephalopathy. MRI abnormalities are characterized by diffuse cortical atrophic changes and by hyperintensity on T2-weighted images in the white matter, basal ganglia, and thalami [71].

Methyl-mercury poisoning (Minamata disease) is a neurological illness caused by the ingestion of contaminated seafood and characterized by ataxia, visual loss, and sensory disturbance. MRI in affected patients demonstrates atrophy of the cerebellar vermis and hemispheres, as well as the calcarine cortex [72,73].

Metronidazole (Flagyl)-induced cerebellar toxicity is associated with symptoms of ataxia, with MRI findings of increased T2 signal intensity and restricted diffusion in

the dentate nuclei [74]. With symptom resolution MRI becomes normal [74].

In central pontine myelinolysis (osmotic demyelination syndrome), cerebellar or extrapyramidal symptoms have been observed. More typically, patients demonstrate coma, locked-in syndrome, or quadriplegia. This disorder is typically seen in chronic alcoholics or malnourished patients following the rapid correction of hyponatremia. Increased T2 signal intensity in the pons is the characteristic finding [75].

A leukoencephalopathy with initial symptoms of ataxia has also been reported to occur in association with the chronic inhalation of heroin vapors [71].

Vitamin E deficiency can occur in association with several acquired gastrointestinal disorders or with autosomal recessive defects in vitamin E transport [76,77]. Symptoms include ataxia with associated weakness, areflexia, and retinal degeneration. Imaging has demonstrated cerebellar atrophy and increased T2 signal intensity in the posterior columns of the spinal cord [76,77].

Chronic ethanol abuse is associated with ataxia and multiple other symptoms of neurologic dysfunction. These symptoms result from the neurotoxicity of ethanol and its metabolic products, from associated chronic liver disease, from secondary nutritional deficiencies, and from the effect of other toxins that are simultaneously ingested [75]. MRI demonstrates atrophy of the cerebellar vermis, especially superiorly, as well as volume loss involving pons, medulla, and cerebral hemispheres [75].

Wernicke encephalopathy is due to thiamine deficiency and classically presents with ataxia, altered mental status, and abnormality of ocular motility. MRI demonstrates increased T2 signal intensity, reversible contrast enhancement, and reversible restricted diffusion in multiple areas including mammillary bodies, hypothalamus adjacent to the third ventricle, periaqueductal gray and white matter, pulvinar, and dorsomedial portions of the thalamic nuclei [75]. Small hemorrhagic foci can also be demonstrated in these regions.

Reversible posterior leukoencephalopathy is most commonly characterized by headache, altered consciousness, visual disturbance, and seizures [78]. Ataxia can be a component, especially when there is brainstem or cerebellar involvement [78,79]. Antecedent clinical conditions include hypertension, eclampsia, renal disease, and the use of cytotoxic or immunosuppressant drugs [78]. MRI findings include the presence of bilateral and generally symmetrically increased T2 signal intensity in the posterior parietal and occipital lobes, with apparent

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early restricted and subsequent increased diffusion in these same areas [79].

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