TABLE 114-8 DIFFERENTIAL DIAGNOSIS OF CEREBELLAR ATAXIA

GENETIC DISORDERS	**Autosomal dominant**	Spinocerebellar Ataxias Episodic ataxia DRPLA
	Autosomal recessive	Friedreich's ataxia Ataxia-telangiectasia Ataxia with oculomotor apraxia Ataxia with vitamin E deficiency
	X-linked	Fragile X-associated tremor/ataxia syndrome
	Mitochondrial	Polymerase gamma (POLG)
ACQUIRED/ SPORADIC	**Medications/Toxins**	Alcohol Phenytoin Fluorouracil Heavy metals Carbon monoxide
	Developmental	Chiari malformations Dandy-Walker malformations Pontocerebellar hypoplasia
	Immune mediated	Paraneoplastic (anti-Hu/Yo/Ri) Pediatric post-viral Behçhet's disease
	Infectious	HIV/AIDS PML CJD Lyme disease
	Metabolic	Thiamine deficiency (Wernicke's encephalopathy) vitamin E/B12 deficiency Thyroid disease
	Vascular	Cerebellar stroke/hemorrhage
	Neoplastic	Primary and metastatic tumors Paraneoplastic (anti-Hu/Yo/Ri)
	Miscellaneous	MSA-cerebellar Multiple sclerosis

CJD, Cruetzfeldt-Jakob disease; DRPLA, dentatorubropallidoluysian atrophy; MSA, multiple system atrophy; PML, progressive multifocal leukoencephalopathy.

cognitive, or behavioral features. They are usually adult onset with variable genetic mutations, including trinucleotide repeats, mutations in noncoding regions, and point mutations. Genetic testing is available for many of the common spinocerebellar ataxias and new mutations are being identified in a rapid and ongoing basis. Currently there are no treatments to address disease progression and symptomatic treatment is limited.

The fragile X mental retardation (FMR1) gene contains a CCG trinucleotide repeat expansion of greater than 200 in the fully penetrant mutation associated with mental retardation in boys. Recently a pre-mutation associated with repeats of 55-200 in the FMR1 gene has been found to be the cause of the adult onset neurodegenerative disorder, fragile X–associated tremor/ataxia syndrome (FXTAS). Clinically, affected males have a progressive cerebellar tremor and ataxia. Fragile X–associated tremor/ataxia syndrome has been under-recognized and may be the most common genetic cause of late onset ataxia. Treatment is largely symptomatic and the disease results in progressive disability.

Autosomal recessive ataxias are rare conditions with onset in childhood. Friedreich's ataxia (FA) is the most common and best characterized of these disorders. It results from an unstable GAA expansion on chromosome 9. Clinically it is characterized by childhood onset gait ataxia and clumsiness. The ataxia reflects a combination of spinocerebellar degeneration and peripheral sensory loss. Frank weakness secondary to pyramidal tract dysfunction is a late complication. Non-neurological manifestations include cardiomyopathy, diabetes mellitus, and skeletal deformities, which add to the morbidity and mortality of the disease. Since identification of the mutation, late onset forms of the disease with less systemic involvement and milder symptoms have been identified. Therefore, Friedreich's ataxia should be considered in the differential of adult onset sporadic ataxias.

Ataxia with vitamin E deficiency is a childhood onset ataxia with a Friedreich's ataxia phenotype. Treatment with high dose vitamin E may slow the progression of neurological symptoms. Ataxia with vitamin E deficiency should be considered in any child with signs and symptoms of Friedreich's ataxia that do not carry the Friedreich's ataxia mutation.

Sporadic/Acquired Ataxias

Insidious onset of cerebellar ataxia without a family history can be a diagnostic challenge. Alcohol abuse, toxins, multiple system atrophy, and mitochondrial disorders are diagnostic considerations.

Acute or subacute onset ataxia is most often associated with cerebrovascular disease, demyelinating illness, or direct or indirect effects of cancer. Paraneoplastic cerebellar degeneration is one of the more common paraneoplastic syndromes usually associated with gynecological, breast, lung cancer, or lymphoma. A variety of anti-neuronal antibodies have been implicated; however, anti-Hu/Yo/Ri are most frequently seen. The cerebellar syndrome often predates the identification of the cancer. Treatment of the underlying cancer and plasma exchange are sometimes beneficial.

Vitamin B12 and vitamin E deficiency secondary to malabsorption can present with ataxic gait as a result of posterior column sensory deficits. In the appropriate clinical situation, Wernicke's encephalopathy due to thiamine deficiency needs to be considered as an acute cause of gait ataxia.

SUGGESTED READINGS

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