The term ataxia refers to a special disorder of movement resulting from lesions of the cerebellum or spinocerebellar tracts. The disorders, which result in ataxia in children, are somewhat different from those in adults. Signs of ataxia in children may be detected as early as the first year of life. This is especially apparent when the child sits down and reaches for objects. Ataxias of childhood can be categorized initially by ascertaining the following: 1) whether this is an acute, acute recurrent, or chronic disorder; 2) if chronic, whether it is a progressive or static disorder; and 3) whether this is a symptom of cerebellar, posterior column, or vestibular dysfunction.

In adolescents, the manifestations of cerebellar ataxia are similar to those in adults and are associated with other signs of cerebellar dysfunction (dysdiadochokinesis, dyssynergia, etc.). The diagnosis may be more difficult in younger children, and care must be taken before ascribing minor problems of gait and stance to cerebellar disorders. Sensory ataxia in older children can be detected as in adults when Romberg sign is present. Severe sensory ataxia can sometimes be detected early in life in conditions such as Dejerine-Sottas disease by the ability to correct posture with eyes open but not with eyes closed.

**ACUTE AND ACUTE EPISODIC ATAXIA**

**Infectious and Postinfectious**

Acute cerebellar ataxia in children most often follows an infectious process. Varicella-zoster virus infection is most often implicated. Other viruses can produce a similar picture [Epstein-Barr virus (1), Coxsackievirus, and other enteroviruses, etc.]. The onset is sudden and can occur immediately or as late as 6 weeks after the viral illness. Cerebrospinal fluid examination may show mild pleocytosis. The course is usually benign (2). Complications can sometimes rise because of cerebellar swelling, with development of obstructive hydrocephalus (3–6). If there are other neurological signs, imaging should be obtained to evaluate for strokes and mass lesions.

**Drugs**

A number of drugs can cause acute ataxia, often associated with nystagmus, drowsiness, and vomiting. Intoxication with benzodiazepines, barbiturates, phenytoin, phenothiazines, and carbamazepines are well known to cause ataxia.
Vascular Causes

Basilar migraine, vascular occlusions, malformations arising from vertebral or basilar arteries, and cerebellar hematomas can cause ataxia. Asymmetrical ataxia is present on the side of unilateral cerebellar involvement.

Miller-Fisher Syndrome

The Gullain-Barré syndrome and its variants can manifest as acute ataxia in children. On closer examination, other manifestations such as muscle weakness, hypotonia, and areflexia are usually present. Cerebrospinal fluid examination will show elevated protein with normal cell count. The GQ1 antibody test is positive in the Miller-Fisher variant.

Posterior Fossa Tumors and Abscess

More than 50% of the brain tumors in childhood occur in the posterior fossa (7). Posterior fossa tumors, including cerebellar astrocytoma, brain stem glioma, and medulloblastoma, can present with acute ataxia (8). There may be evidence of increased intracranial pressure. The prognosis for these childhood tumors has improved greatly in recent times with early diagnosis and treatment (9). Thus, it is imperative to get imaging studies in suspicious cases.

Episodic Ataxias

Recurrent episodic ataxia in childhood may be a manifestation of a number of hereditary metabolic disorders (10). The ataxia may be precipitated by an acute infection or during recovery. There may be associated lethargy and vomiting. Some of the better known examples are maple syrup urine disease, Hartnup disease, and Leigh disease. Several other lesser known aminoacidopathies and organic acidemias also may present with acute ataxia.

Hereditary Episodic Ataxia

This disease is inherited in an autosomal-dominant manner and is characterized by paroxysmal bouts of ataxia, dysarthria, and nystagmus. Ataxia is often severe. Between episodes, electroencephalograms, caloric testing of vestibular function, and serum chemistry are normal (11). Cerebellar vermician atrophy has been reported in long-standing cases. Hereditary episodic ataxia is now classified into two groups and is the result of mutations of genes that code for ion channels. In EA1, a disease characterized by episodes of ataxia provoked by movement and startle, missense mutations in a potassium channel gene KCNA1 have been found. Patients with EA2, another form of paroxysmal ataxia, carry mutations of the gene encoding for the α1A voltage-dependent calcium channel subunit CACNA1A that are predicted to result in truncated channel proteins (12). Episodic ataxia responds to acetazolamide.

CONDITIONS THAT MAY BE ASSOCIATED WITH ACUTE ATAXIA

Opsoclonus-Myoclonus syndrome

This syndrome of dancing eyes, acute incoordination, and muscle jerks may be associated with acute ataxia. It is important to recognize this syndrome, as it may be associated with neuroblastoma (13). Opsoclonus-myoclonus may sometimes be associated with varicella and other viral infections and sometimes may be idiopathic. The prognosis ranges from complete recovery to persistence for several years and seems independent of etiology. This syndrome may persist after removal of the neuroblastoma. Patients may respond to adrenocorticotropic hormone or prednisone therapy.

Chronic Progressive Ataxias of Childhood

Chronic progressive ataxias may be hereditary or acquired. Ataxia is rarely an isolated manifestation of hereditary metabolic disease. The prototype of hereditary ataxia is Friedreich ataxia. Other conditions include ataxia-telengectasia, vitamin E deficiency, abetalipoproteinemia, Refsum’s disease, and late infantile and juvenile sphingolipidosis.

Friedreich Ataxia

Friedreich ataxia is a trinucleotide repeat disorder that is inherited in an autosomal-recessive manner. The trinucleotide repeat is GAA, and most patients have a range of 600 to 900 repeats. The gene is localized to chromosome 9q (14) and regulates the synthesis of a protein called fraxatin. When direct molecular testing became available for Friedreich ataxia, up to 10% of patients who did not fulfill the criteria for Friedreich ataxia tested positive (15). Friedreich ataxia is the most frequently inherited ataxia in Caucasians.

Most commonly, the onset of Friedreich ataxia occurs at the beginning of puberty (16), but earlier as well as later onset has been reported. Progressive unrelenting ataxia with mixed cerebellar and sensory features is the cardinal feature of this disease. Truncal ataxia is usually the first symptom, followed by incoordination, dysmetria, and intention tremor. A progressive dysarthria appears soon after onset (17). Muscular weakness is common and progressive. There is an axonal sensory neuropathy resulting in sensory loss and loss of deep tendon reflexes. Loss of tendon reflexes was considered essential for the diagnosis in the past; however, it recently has been noticed that a minority of patients may have preserved and even exaggerated tendon reflexes (18). The plantar re-
flexes are extensor because of involvement of the pyramidal tract. Extensor plantar responses were in the past considered essential to make the diagnosis (19). It now is known that exceptions to these rules can occur. Position and vibration sensations are reduced. Optic atrophy occurs in 30% of patients (20). Sensorineural hearing loss occurs in 20% of patients. Friedreich considered degeneration of the posterior column as the cardinal pathological feature. Other pathological changes in the nervous system include degeneration of the dorsal root ganglion and corticospinal and spinocerebellar tracts.

Other features include kyphoscoliosis, pes cavus, and pes equinovarus (21). Cardiomyopathy is present in 50% of cases. In most patients, heart disease remains asymptomatic, but it can contribute to disability and premature death (22). About 10% of patients develop diabetes mellitus. Neuroimaging reveals thinning of the cervical spinal cord with abnormal signals in the posterior and lateral columns on sagittal and axial magnetic resonance imaging in almost all patients with Friedreich ataxia (23, 24).

**Ataxia-Telengeictasia**

Ataxia-telengeictasia is an autosomal-recessive disorder first described by Syllaba and Henner (25) and Louis Barr (26). The onset is in childhood with ataxia, choreoathetosis, oculocutaneous telengeictasia, immunological deficiency, increased frequency of malignancies, and endocrine abnormalities. Recurrent infections are common, with reduced immunoglobulins (Ig) A, IgE, and IgG2. The gene has been localized to chromosome 11q22–23 (27). Neurological symptoms can appear at as early as 12 to 18 months of age. Ataxia is usually the first symptom, followed by dysarthria. The disease progresses slowly. The incidence of malignancies has been estimated to be 38% (28). Elevated carinoembryonic antigen is present. Cytogenetic abnormalities indicating chromosomal instability are frequent. In cell cultures, there is an increased sensitivity of the patient’s chromosomes to x-radiation.

**Abetalipoproteinemia (Bassen-Kornzweig Syndrome)**

Bassen and Kornzweig (29) first described abetalipoproteinemia in 1950. It is a recessively inherited disease characterized by the virtual absence of apolipoprotein B and apolipoprotein B-containing lipoproteins in plasma. Microsomal triglyceride transfer protein, a resident lipid transfer protein within the endoplasmic reticulum of hepatocytes and enterocytes, is absent in affected individuals (30). The first symptom is fat malabsorption. Ataxia develops at about 5 to 10 years of age. Areflexia, proprioceptive disturbance, and cerebellar signs constitute the usual syndrome. Acanthocytosis is a constant finding. Extensor plantar responses were in the past considered essential to make the diagnosis (19). It now is known that exceptions to these rules can occur. Position and vibration sensations are reduced. Optic atrophy occurs in 30% of patients (20). Sensorineural hearing loss occurs in 20% of patients. Friedreich considered degeneration of the posterior column as the cardinal pathological feature. Other pathological changes in the nervous system include degeneration of the dorsal root ganglion and corticospinal and spinocerebellar tracts.

Vitamin E Deficiency

Vitamin E deficiency is an important cause of ataxia, peripheral neuropathy, or both. In most cases, it is caused by malabsorption. An isolated ataxia with vitamin E deficiency in the absence of malabsorption also has been described (31). This is one of the few reversible metabolic ataxias in childhood, and, hence, there is the need to measure vitamin E levels in all cases of unexplained ataxia. Ataxia with isolated vitamin E deficiency is an autosomal-recessive disease with a defect in the liver of α-tocopherol transfer protein. The ataxia with isolated vitamin E deficiency locus has been mapped to chromosome 8q13 (32–34). Onset of disease is in the first or second decade, and it is indistinguishable from Friedreich ataxia. Areflexia, dysarthria, and proprioceptive loss are common. Low fasting vitamin E levels in the presence of normal vitamin E absorption suggest diagnosis. This can be demonstrated by vitamin E tolerance tests. Treatment with 800 to 900 IU of oral DL-α-tocopheral stabilizes or improves neurological status.

**Refsum’s Disease**

Refsum’s disease is an autosomal-recessive disorder with a genetic defect in the α-oxidation of phytanic acid (35). The tetrad of symptoms includes cerebellar ataxia, retinitis pigmentosa, chronic progressive demyelinating sensory-motor polyneuropathy, and elevated cerebrospinal fluid protein concentration. Age of onset is variable, and symptoms may be present in early infancy. There is a high incidence of deafness. Phytanic acid levels are elevated in serum and urine. A Refsum’s disease gene, phytanoyl-CoA hydroxylase (PAHX), has been localized to chromosome 10p13 between the markers D10S226 and D10S223 (36). The clinical course can be improved by restricting phytic acid in the diet. Therapeutic plasma exchange has been shown to be particularly useful for rapidly lowering plasma phytic acid levels during acute attacks and may play a significant role as a maintenance therapy as well (37). It must be remembered that infantile Refsum’s disease is a completely different entity characterized by loss of multiple peroxisomal metabolic functions. Phytic acid can accumulate in peroxisomal disorders,
probably because peroxisomes play a role in phytic acid metabolism (38).

**Sensory Ataxia**

Subacute degeneration of the spinal cord may be taken as a prototype of sensory ataxia. In children, this may result from familial malabsorption of cobalamin or from inborn errors of folate or cobalamin metabolism (39). Although rare, childhood pernicious anemia is a treatable disease that should be included in the differential diagnosis of the sensory ataxias in children (40). Loss of proprioception and vibration sensation leads to sensory ataxia and a positive Romberg sign. Motor signs include loss of strength, spasticity, and extensor plantar responses. Visual impairment may occur. Serum vitamin B12 levels are normal in children with inborn errors of folate or cobalamin synthesis. Early diagnosis and treatment may prevent permanent neurological damage. It is important to remember that megaloblastic anemia may be absent in genetic errors of folate and cobalamin synthesis. Homocystinuria is present. Mental changes and developmental delay may be present. Sensory ataxia may occasionally be present in hereditary polyneuropathies.

**Carbohydrate-Deficient Glycoprotein Syndrome**

Carbohydrate-deficient glycoprotein syndrome is a newly delineated group of inherited multisystemic disorders associated with abnormal glycosylation of a number of serum glycoproteins. Several types have been described on the basis of clinical presentation and biochemical changes (41). Patients with carbohydrate-deficient glycoprotein syndrome type la usually present with neurological (hypotonia, strabismus, and cerebellar hypoplasia) and cutaneous (inverted nipples and abnormal distribution of adipose tissue) abnormalities, together with multivisceral involvement (digestive, hepatic, cardiac, and renal). In childhood, the prominent features include cerebellar ataxia, mental retardation, retinitis pigmentosa, and peripheral neuropathy. Computed tomography and magnetic resonance imaging show cerebellar atrophy and pathological changes include olivopontocerebellar atrophy, hepatic micronodular cirrhosis, and renal microcysts.

A number of other hereditary and metabolic diseases may have ataxia as a primary or associated manifestation. This group includes autosomal-dominant spinocerebellar ataxia and cerebellar ataxia (predominantly adult), Lafora disease, Leigh disease, and a number of late infantile and juvenile sphingolipidoses. Other conditions to be considered in chronic progressive ataxia include tumors of the cerebellum and subacute encephalitis. Long-standing hydrocephalus also may present with unsteady gait.

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**THE CHRONIC NONPROGRESSIVE ATAXIAS**

**Ataxic Cerebral Palsy**

A form of cerebral palsy with predominant ataxia is well known. These patients are hypotonic docile infants with delayed speech and motor skills. Ataxic cerebral palsy accounts for 5% to 10% of all forms of cerebral palsy, and it is estimated that approximately 50% of ataxic cerebral palsy is inherited as an autosomal-recessive trait. Recently, the genetic locus has been mapped in a family to chromosome 9p12-q12. (42). The identification of genes involved in the etiology of cerebral palsy will offer the possibility of prenatal/premarital testing to some families with children affected with the disorder and will greatly increase our understanding of the development of the control of motor function. Mental retardation often is associated, leading to questions about the role of the cerebellum in cognitive functions (43). Patients may present with the disequilibrium syndrome described by Hagberg and colleagues (44). Before making this diagnosis, genetic diseases must be ruled out.

**Other Nonprogressive Cerebellar Ataxias in Childhood**

A form of olivopontocerebellar atrophy has been described in adolescents. Congenital pontocerebellar aplasia is probably a different disorder. The vermis is preserved in this condition. An inherited form of idiopathic cerebellar ataxia also has been described. It is not clear if these are definite entities or phenotypical variants of other more common cerebellar disorders.

**APPROACH TO DIAGNOSIS**

There is a diverse group of conditions that can give rise to ataxia in childhood, but with a systematic approach the possibilities can be significantly narrowed down, and investigations can be directed toward the most likely diagnosis.
Acute Ataxias

A history of viral illness, especially varicella-zoster virus infection or drug ingestion, may point toward the etiology. The highest diagnostic yield is from a drug screen and cerebrospinal fluid examination. In one study, 80% of children who presented with ataxia had a discharge diagnosis of drug-induced or postviral ataxia or Gullain-Barre syndrome (45). However, the presence of other neurological signs would indicate the need for imaging and other studies. The presence of headache, vomiting, and other signs of raised intracranial pressure would make imaging mandatory. Vertebrobasilar disease, strokes, and basilar migraine are other important considerations (Table 1).

Intermittent or Episodic Ataxia

There are two important considerations here. Hereditary episodic ataxia is a channelopathy and may respond to acetazolamide. The other important consideration is metabolic diseases presenting with intermittent ataxia. A variant form of maple syrup urine disease leading to intermittent branch chain ketoaciduria, ataxia, and lethargy is known. Other well-known metabolic diseases associated with ataxia are Hartnup disease, Leigh disease, pyruvate carboxylase deficiency, and biotidinase deficiency. The presence of lethargy and vomiting and raised intracranial pressure should raise the suspicion of a metabolic disease. Benign paroxysmal vertigo of childhood may present with a symptom complex characterized by attacks of vertigo in young children combined with nystagmus, ataxia, and transiently decreased vestibular function but without impaired consciousness. Diagnostic and follow-up studies reveal a close relationship to migraine (Table 2).

Chronic Ataxia

The most important considerations here are the progression of the disease process and associated signs. A static ataxia represents either an inherited condition or a cerebral palsy. The inherited form is a heterogeneous group including such conditions as olivopontocerebellar atrophy (a predominantly adult condition) to cerebellar atrophy with Werdnig-Hoffmann disease seen in children (46). Before making a diagnosis, pure ataxic cerebral palsy and hereditary metabolic conditions must be ruled out in the young child (Table 3). Chronic progressive ataxias are important to recognize. Some of them are potentially treatable, such as ataxia with vitamin E deficiency and Refsum’s disease. Most can be diagnosed by genetic or biochemical studies. It is important to remember that ataxia is almost never an isolated symptom in metabolic or hereditary disease. Progressive ataxias also may be a manifestation of slow-growing brain tumors and

<table>
<thead>
<tr>
<th>Disease</th>
<th>Diagnostic Features/Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute cerebellar ataxia</td>
<td>History of varicella-zoster/other viral infection</td>
</tr>
<tr>
<td></td>
<td>CSF pleocytosis</td>
</tr>
<tr>
<td>Drugs</td>
<td>History of drug ingestion</td>
</tr>
<tr>
<td></td>
<td>Blood drug levels</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>Hyptonia, areflexia</td>
</tr>
<tr>
<td></td>
<td>Elevated protein in cerebrospinal fluid with normal cell count</td>
</tr>
<tr>
<td>Cerebellar tumors</td>
<td>Headache, vomiting, pappiledema</td>
</tr>
<tr>
<td></td>
<td>Magnetic resonance imaging/computed tomography posterior fossa tumor</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease</th>
<th>Diagnostic Features/Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary episodic ataxia</td>
<td>Family history</td>
</tr>
<tr>
<td></td>
<td>Response to acetazolamide</td>
</tr>
<tr>
<td></td>
<td>Patients normal in between attacks</td>
</tr>
<tr>
<td></td>
<td>Mutations in genes encoding for channels</td>
</tr>
<tr>
<td>Metabolic diseases</td>
<td>Vomiting and lethargy precipitated by infection</td>
</tr>
<tr>
<td></td>
<td>Urine, blood for metabolic screen</td>
</tr>
<tr>
<td></td>
<td>Nystagmus, vestibular dysfunction</td>
</tr>
<tr>
<td></td>
<td>No loss of consciousness</td>
</tr>
<tr>
<td>Benign paroxysmal vertigo</td>
<td>Migraine variant</td>
</tr>
</tbody>
</table>
subacute encephalopathies, and imaging and cerebrospinal fluid examination may be required for diagnosis.

CONCLUSION

Ataxias in childhood may be a manifestation of a wide-ranging category of diseases. It may be a manifestation of vestibular disturbance, cerebellar disease, or posterior column disease. Diagnosis may be approached with a chronological division into acute, episodic/recurrent, and chronic ataxia. Chronic ataxias may be further divided into static and progressive conditions. Many of the specific entities may be suspected on the basis of associated symptoms and signs. Even in the young child, it may be possible to differentiate cerebellar from posterior column involvement. A systematic approach may enhance diagnostic accuracy.

REFERENCES


Table 3.

Approach to Diagnosis of Chronic Ataxia

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical Features</th>
<th>Laboratory Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedreich ataxia</td>
<td>Progressive ataxia with mixed cerebellar and sensory features, sensory loss, loss of deep tendon reflexes</td>
<td>Pes cavus, upward plantar, cardiomegaly, diabetes</td>
</tr>
<tr>
<td></td>
<td>Variable phenotype with ataxia most constant feature</td>
<td>Hyperexpansion of GAA trinucleotide repeat</td>
</tr>
<tr>
<td>Ataxia-telangiectasia</td>
<td>Ataxia, oculocutaneous telangiectasia, immunological deficiencies, increased risk of malignancies</td>
<td>Reduced IgG2, IgA, IgE, Elevated AFP, CEA, chromosomal instability</td>
</tr>
<tr>
<td>Abetalipoproteinemia (Bassen-Kornzweig syndrome)</td>
<td>Fat malabsorption, areflexia, proprioceptive disturbances, acanthocytosis, cardiomegaly</td>
<td>Absent apolipoprotein B</td>
</tr>
<tr>
<td>Vitamin E deficiency</td>
<td>Hereditary or with fat malabsorption</td>
<td>Low fasting Vitamin E levels</td>
</tr>
<tr>
<td>Refsum’s disease</td>
<td>Retinitis pigmentosa, deafness, peripheral neuropathy</td>
<td>Elevated cerebrospinal fluid protein and blood phytic acid</td>
</tr>
<tr>
<td>Subacute combined degeneration of the spinal cord</td>
<td>Loss of proprioception, vibration</td>
<td>Sensory ataxia, spasticity, Homocystinuria present</td>
</tr>
<tr>
<td></td>
<td>Vitamin B12 levels may be normal</td>
<td>Reversible</td>
</tr>
</tbody>
</table>

IG = immunoglobulin; AFP = alpha-feto protein; CEA = carcinomaembrionic antigen.