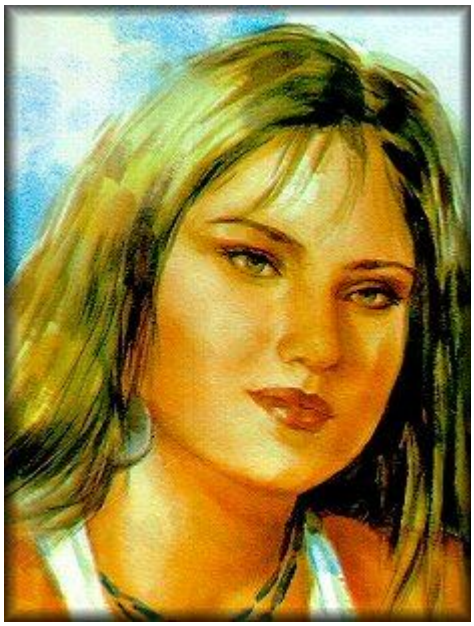
ATAXIA

Dr.M. YASSER METWALLY

INDEX



- **INTRODUCTION**
- **ACUTE RECURRENT ATAXIA**
- **CHRONIC PROGRESSIVE ATAXIA**
- **PHARMACOLOGICAL MANAGEMENT OF CEREBELLAR DEFICITS**

ATAXIA

The term "ataxia" can be used for any disturbance in gait but is used here in a more restricted sense to denote disturbances of coordination rather than strength. Disturbances of coordination are typically caused by dysfunction of the cerebellum or its major input systems from the frontal lobes or the posterior columns of the spinal cord. An ataxic gait is wide based, lurching, and staggering, and in the observer it provokes fear that the patient is in danger of falling. The same gait is seen in people who are attempting to walk in a vehicle that has several directions of movement at once, such as a train. When an abnormality occurs in the vermis of the cerebellum, the child cannot sit still but constantly moves the body to and fro and bobs the head (titubation). In contrast, disturbances of the cerebellar hemispheres cause a tendency to veer in the direction of the affected hemisphere, with dysmetria and hypotonia in the ipsilateral limbs. Bifrontal lobe disease may produce symptoms and signs indistinguishable from cerebellar disease.

Table 1. Acute or Recurrent Ataxia

- **Brain Tumor**
- **Conversion Reaction**

- **Drug Ingestion**
- **Encephalitis (brainstem)**
- **Genetic Disorders**
  - **1. Carnitine acetyltransferase deficiency**
  - **2. Dominant recurrent ataxia**
  - **3. Hartnup disease**
  - **4. Maple syrup urine disease**
  - **5. Paroxysmal ataxia and myokymia**
  - **6. Pyruvate decarboxylase deficiency**
- **Migraine**
  - **1. Basilar**
  - **2. Benign paroxysmal vertigo**
- **Postinfectious Immune**
  - **1. Acute postinfectious cerebellitis**
  - **2. Miller-Fisher syndrome**
  - **3. Myoclonic encephalopathy and neuroblastoma**
  - **4. Multiple sclerosis**
- **Pseudoataxia (epileptic)**
- **Trauma**
  - **1. Hematoma**
  - **2. Postconcussion**
  - **3. Vertebrobasilar occlusion**
- **Vascular Disorders**
  - **1. Cerebellar hemorrhage**
  - **2. Kawasaki disease**
  - **3. Lupus erythematosus**

Loss of sensory input to the cerebellum, because of peripheral nerve or posterior column disease, necessitates constant looking at the feet to know their location in space. The gait is also wide based but is not so much lurching as careful. The foot is raised high with each step and slaps down heavily on the ground. Station and gait are considerably worse with the eyes closed, and the patient may actually fall to the floor (positive Romberg sign).

The differential diagnosis of a child with acute ataxia or recurrent attacks of ataxia (Table 1) is quite different from that of a child with chronic static or progressive ataxia (Table 2). Therefore these two presentations are discussed separately in the text. However, the reader must remember that a slowly progressive ataxia may be noticed "acutely" and that children with recurrent ataxia may never return to baseline after each attack and may have a progressive ataxia superimposed on the acute attacks.

Table 2. Chronic or Progressive Ataxia

- **Brain Tumors**
  - **1 -Cerebellar astrocytoma**
  - **2. Cerebellar hemangioblastoma (von Hippel-Lindau disease)**
  - **3. Ependymoma**
  - **4. Medulloblastoma**
  - **5. Supratentorial tumors**
- **Congenital Malformations**
  - **1. Basilar impression**
  - **2. Cerebellar aplasias**
    - **a. Cerebellar hemisphere aplasia**
    - **b. Dandy-Walker malformation**
    - **c. Vermial aplasia**
  - **3. Chiari malformation**
- **Hereditary Ataxias**
  - **1. Autosomal dominant inheritance**
    - **a. Machado-Joseph disease**
    - **b. Olivopontocerebellar degeneration**
    - **c. Ramsay Hunt syndrome**
      - **1. With pallidoluysian atrophy**
      - **2. With mitochondrial myopathy**

- **2. Autosomal recessive inheritance**
  - **a. Abetalipoproteinemia**
  - **b. Ataxia-ocular motor apraxia**
  - **c. Ataxia-telangiectasia**
  - **d. Ataxia with episodic dystonia**
  - **e. Friedreich ataxia**
  - **f. Harding ataxia**
  - **g. Hartnup disease**
  - **h. Hypobetalipoproteinemia**
  - **i. Juvenile GM2 gangliosidosis**
  - **j. Juvenile sulfatide lipidoses**
  - **k. Maple syrup urine disease**
  - **1. Marinesco-Sjogren syndrome**
  - **m. Pyruvate dysmetabolism**
  - **n. Ramsay Hunt syndrome**
  - **o. Refsum disease (HSMN IV)**
  - **p. Respiratory chain disorders**
  - **q. Sea-blue histiocytosis**
- **3. X-linked inheritance**
  - **a. Adrenoleukodystrophy**
  - **b. Leber optic neuropathy**
  - **c. Adult-onset dementia**

ACUTE RECURRENT ATAXIA

The two most common causes of ataxia among children who were previously healthy and then suddenly have an ataxic gait are drug ingestion and acute postinfectious cerebellitis (Table 1). Migraine, brainstem encephalitis, and an underlying neuroblastoma are the next considerations.

In preadolescent and adolescent girls a conversion reaction is always a possibility. Recurrent ataxia is uncommon and is usually caused by hereditary disorders; migraine is the most common cause, and disorders of pyruvate metabolism are second.

- **Brain tumours**

Primary brain tumors ordinarily produce chronic progressive ataxia and are discussed later in the chapter. However, tumors may also be manifested as acute ataxia because of bleeding, sudden shifts in position that cause hydrocephalus, or growth. In addition, clumsiness may be overlooked until it becomes severe enough to cause an obvious gait disturbance. For this reason, brain imaging is recommended for all children with acute cerebellar ataxia.

- **Conversion reaction**

Clinical Features. Hysterical gait disturbances are common in children, especially girls between 10 and 15 years of age. The disturbance is involuntary, usually provides a secondary gain such as attention, and should be distinguished from malingering, which is a voluntary act. Hysterical gait disturbances are often extreme and if so are named astasia-abasia. The child appears to sit without difficulty but when brought to standing immediately begins to sway from the waist. The child does not assume a wide-based stance to increase stability. Instead the child lurches, staggers, and otherwise travels across the room from object to object. The lurching maneuvers are often complex and require extraordinary balance. Strength, tone, sensation, and tendon reflexes are normal.

Diagnosis. Hysterical gait disturbances are usually diagnosed by observation; laboratory tests are not ordinarily required to exclude other possibilities.

Treatment. Determination of the precipitating stress is important. Conversion may represent a true call for help in a desperate situation such as child abuse. Such cases require referral to a multispecialty team able to deal with the whole family.

Most children with hysterical gait disturbances are responding to a more immediate and less serious difficulty. Symptoms can usually be treated by the use of suggestion and do not require psychiatric referral except when conversion is used repeatedly to handle stress.

- **Drug ingestion**

The incidence of accidental drug ingestion is highest between I and 4 years of age.

Clinical Features. An overdose of most psychoactive drugs can produce ataxia, which is usually associated with some change in personality or sensorium. Toxic doses of anticonvulsant drugs, especially phenytoin, may produce marked ataxia without an alteration in sensorium. Nystagmus usually is present as well. Excessive use of antihistamines in the treatment of an infant or young child with allergy or an upper respiratory infection may produce ataxia. This is especially true in children with otitis media, who may have underlying unsteadiness because of middle ear infection. Other drugs and toxins that can induce cerebellar ataxia are listed in box 1.

Box 1. Ataxia due to drugs and toxins ingestion .

- **Heavy metal intoxications.**

- Mercury, Lead, thallium, solvents.

- **Drugs and medications.**
  - Toxic doses of anticonvulsant drugs, especially phenytoin and carbamazepine.
  - Barbiturates and benzodiazepines, lithium.
  - Ethanol intoxication (alcoholism).
  - Chemotherapeutic agents.
    - 5 fluorouracil
    - Methotrexate
    - Cyclosporine
    - Cytosine arabinoside

Diagnosis. The parents or care providers of every child with acute ataxia should be carefully questioned concerning drugs intentionally administered to the child and other drugs accessible in the home. It is worthwhile to inquire specifically if anyone in the family is using anticonvulsant or psychoactive drugs. Urine should be screened for drug metabolites, and blood should be sent for analysis when a specific drug is suspected.

Treatment. Treatment depends on the specific drug ingested and its blood concentration. In most cases of ataxia caused by drug ingestion, the drug can be safely eliminated spontaneously if vital function is not compromised, if acid-base balance is not disturbed, and if liver and kidney function is normal. In life-threatening situations dialysis may be necessary while vital function is supported in an intensive care unit.

Management of acute cerebellar ataxia

Positive Family History	Migraine, Dominant Recurrent Ataxia, Metabolic Errors
Negative	
Drug Screen CT or MRI	Intoxication, Brain Tumor, Hemorrhage
Negative	
Lumbar puncture	Encephalitis, Miller Fisher, Multiple Sclerosis
Negative	
HVA/VMA MRI of Chest and Abdomen	Neuroblastoma, Myoclonic Encephalopathy
Negative	
Glucose-Lactate Tolerance Amino Acid Analysis	Metabolic Errors
Negative	
Electroencephalogram	Pseudoataxia (epilepsy), Acute cerebellar ataxia.

- **Encephalitis (Brain stem)**

Ataxia may be the initial feature of viral encephalitis affecting primarily the structures of the posterior fossa. Echoviruses, coxsackieviruses, and adenoviruses have been implicated as etiologic agents.

Clinical Features. Cranial nerve dysfunction is often associated with the ataxia. A more diffuse encephalitis characterized by declining consciousness and seizures may develop later. Meningismus is sometimes present. The course is variable, and although most children recover completely, some are left with considerable neurologic impairment. Those who have only ataxia and cranial nerve palsies, with no disturbance of neocortical function, tend to recover best. Such cases cannot be distinguished from the Miller-Fisher syndrome on clinical grounds alone.

Diagnosis. Diagnosis requires the demonstration of a cellular response, primarily mononuclear leukocytes, in the cerebrospinal fluid, with or without some elevation of the protein content. Prolonged interpeak latencies of the brainstem auditory evoked response are evidence of an abnormality within the brainstem parenchyma and not the peripheral sensory input system. The electroencephalogram (EEG) is usually normal in children with brainstem encephalitis who have a normal sensorium. A mild increase in theta activity may be recorded as well.

Treatment. No specific treatment is available for viral infection.

- **Migraine**
    - **Basilar Migraine**

The term "basilar (artery) migraine" is used to characterize recurrent attacks of brainstem or cerebellar dysfunction that occur as a manifestation of migraine. Girls are affected more often than boys. The peak incidence is during adolescence, but attacks may occur at any age (Lapkin and Golden, 1978). Infant-onset cases are more Rely to be manifested as benign paroxysmal vertigo.

Clinical Features. Gait ataxia occurs in approximately 50% of patients. Other symptoms include visual loss, vertigo, tinnitus, alternating hemiparesis, and paresthesias of the fingers, toes, and comers of the mouth. An abrupt loss of consciousness, usually lasting only a few minutes, may be reported. Cardiac arrhythmia and brainstem stroke are rare life-threatening complications. Neurologic disturbances are usually followed by a severe, throbbing, occipital headache. Nausea and vomiting occur in less than one third of cases.

Several authors have stressed the association of seizures and occipital lobe spike discharges with attacks of basilar migraine. Such cases should be considered examples of benign occipital epilepsy and not migraine.

Children may have repeated basilar migraine attacks, but with time the episodes evolve into a pattern of classic migraine. Even during attacks of classic migraine the patient may continue to complain of vertigo and even ataxia.

Diagnosis. The diagnosis of basilar migraine, like other forms of migraine, relies heavily on a family history of migraine. An EEG is informative, not only to eliminate the possibility of benign occipital epilepsy, but also because occipital intermittent rhythmic delta activity may be present

during and just after an attack.

Treatment. Many authors have recommended the use of anticonvulsant drugs for basilar migraine. This is probably the result of confusing benign occipital epilepsy with basilar migraine. Prophylactic migraine therapy is indicated in children with basilar migraine.

- **Benign Paroxysmal Vertigo**

Benign paroxysmal vertigo is primarily a disorder of infants and preschool children but may occur in older children.

Clinical Features. Episodes are characterized by the sudden onset of vertigo. True cerebellar ataxia is not present, but vertigo is so profound that posture cannot be maintained. The child either lies motionless on the floor or indicates the need to be held by a parent. Consciousness is not altered, and headache is not reported. The predominant symptoms are pallor, nystagmus, and fright. Episodes last only minutes and may recur at irregular intervals. With time, attacks of paroxysmal vertigo are replaced by episodes of headache and vomiting that are more readily recognized as migraine (Fenichel, 1967).

Diagnosis. The diagnosis is primarily clinical, and laboratory tests are useful only to exclude other possibilities. A family history of migraine, although not necessarily paroxysmal vertigo, can be obtained in almost every case. Some parents indicate that they experience vertigo with their attacks of migraine. Only in rare cases does a parent have a history of benign paroxysmal vertigo.

Treatment. The attacks are so brief and harmless that treatment is seldom indicated. Standard migraine therapy can be employed when the child grows older and vertiginous episodes are replaced by headache and vomiting.

- **Postinfectious immune disorders**

In many of the conditions discussed in this section an altered immune state is blamed for cerebellar dysfunction and. sometimes for other neurologic deficits. Preceding viral infections are usually incriminated but are documented in only half of cases. Considering that children have an average of four to six viral infections a year, it is not surprising that 50% of any group of children have a history of a viral illness during the preceding 30 days. There is no evidence that acute cerebellar ataxia is caused by immunization.

- **Acute Cerebellar Ataxia**

Acute cerebellar ataxia affects children between I and 5 years of age but may occur as late as 14 years. Males and females arc affected equally, and the incidence among family members is not increased.

Clinical Features. The onset is explosive. A previously healthy infant awakens from a nap and cannot stand. Ataxia is maximal at onset. Some worsening may occur during the first hours, but a longer progression, or a waxing and waning course, makes the diagnosis unlikely. Ataxia varies from mild unsteadiness while walking to complete inability to stand or walk. Even when ataxia is severe, sensorium is clear and the child is otherwise normal. Tendon reflexes may be present or absent; their absence suggests Miller-Fisher syndrome. Nystagmus, when present, is usually mild. Chaotic movements of the eyes (opsoclonus) should suggest the myoclonic encephalopathy-neuroblastoma syndrome.

Symptoms may begin to remit after a few days, but complete recovery takes 3 weeks to 5 months. Patients with pure ataxia of the lower limbs and only mild nystagmus are likely to recover completely. Marked nystagmus or opsoclonus (myoclonic encephalopathy), tremors of the head and or moderate irritability is likely to be followed by persistent neurologic sequelae.

Diagnosis. The diagnosis of acute postinfectious cerebritis is one of exclusion. Every child should have drug screening and a brain imaging study. One possible exception is a child in whom ataxia develops during varicella infection. The association between the two is well established, and further diagnostic tests may not be needed. If cranial computed tomography (CT) or MRI findings are normal, lumbar puncture is indicated to exclude encephalitis.

Treatment. Acute postinfectious cerebellitis is a self-limited disease. Treatment is not required.

- **Miller-Fisher Syndrome**

The Miller-Fisher syndrome is characterized by ataxia, ophthalmoplegia, and areflexia. It is generally regarded as a variant of the Guillain-Barre syndrome (Asbury, 1981), although some believe that it may represent a brainstem encephalitis (Al-Din et al, 1982). The disorder is believed to be harmless, and recovery is expected.

Clinical Features. A viral illness precedes the neurologic symptoms by 5 to 10 days in 50% of cases. Either ophthalmoparesis or ataxia may be the initial feature. Both are present early in the course. The most common ocular motor disturbance is paralysis of vertical gaze; upward gaze is more severely affected than downward gaze. The Bell phenomenon may be preserved despite paralysis of voluntary upward gaze, suggesting the possibility of a supranuclear palsy (Meienberg and Ryffel, 1983). Horizontal gaze is generally preserved, but dissociated nystagmus, most marked in the abducting eye, may be present. Ptosis occurs but is less severe than the vertical gaze palsy.

Ataxia is more prominent in the limbs than in the trunk and like the areflexia is probably caused by decreased peripheral sensory input. Weakness of the limbs may be noted. Unilateral or bilateral facial weakness occurs in a significant minority of children. The course is similar to that of Guillain- Barre syndrome. Recovery generally begins 2 to 4 weeks after symptoms become maximal and is complete within 6 months.

Diagnosis. The clinical distinction between the Miller-Fisher syndrome and brainstem encephalitis can be difficult. Disturbances of sensorium, multiple cranial nerve palsies, an abnormal EEG, or prolongation of the interpeak latencies of the brainstem auditory evoked response should suggest a brainstem encephalitis. The cerebrospinal fluid profile in the Miller-Fisher syndrome parallels that of the Guillain-Barre syndrome. A cellular response is noted early in the course, and protein elevation occurs later.

Treatment. Corticosteroids, adrenocorticotrophic hormone (ACTH), and plasmapheresis have not shown benefit in treating the Miller-Fisher syndrome. The outcome in untreated children is excellent.

- **Multiple Sclerosis**

Multiple sclerosis is usually a disease of young adults, but children as young as 24 months have been reported who fulfill the criteria for multiple sclerosis (Bejar and Ziegler, 1984). Whether the childhood forms of multiple sclerosis are etiologically distinct from the adult types has not been determined.

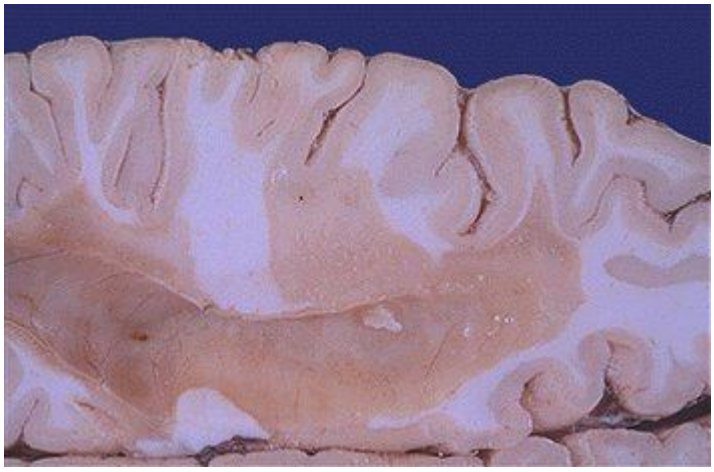


Figure 1. **Seen here in white matter is a large "plaque" of demyelination. The plaque has a grey-tan appearance. Such plaques are typical for multiple sclerosis (MS). These plaques lead to the clinical appearance of transient or progressive loss of neurological function. Since the disease is multifocal and the lesions appear over time, the clinical findings can be quite varied.**

Clinical Features. **The female-to-male ratio varies from 2: l. to 4: 1 (Bouton et al, 1988; Bye et al, 1985). Ataxia, concurrent with a febrile episode, is the most common initial feature in children. Encephalopathy, hemiparesis, or seizures are alternative initial manifestations. Intranuclear ophthalmoplegia that may be unilateral or bilateral develops in one third of patients.**

Clinical features are sufficiently protean that a single prototype cannot be provided. The essential feature is repeated episodes of demyelination in noncontiguous areas of the central nervous system. Each episode is characterized by the rapid development of focal neurologic deficits that persist for weeks and months; afterward the child has partial or complete recovery. Recurrences are separated by months or years and are frequently associated with febrile illnesses. Lethargy, nausea, and vomiting sometimes accompany the attacks in children, but rarely in adults.

The child is usually irritable and demonstrates truncal and limb ataxia. Tendon reflexes are generally brisk throughout. Long-term outcome is unpredictable.

Diagnosis. **Multiple sclerosis may be suspected at the time of the first attack, but definitive diagnosis requires recurrence to establish a polyphasic course. Examination of the cerebrospinal fluid at the time of exacerbation reveals fewer than 25 lymphocytes/mm, a normal or mildly elevated protein content, and sometimes the presence of oligoclonal bands.**

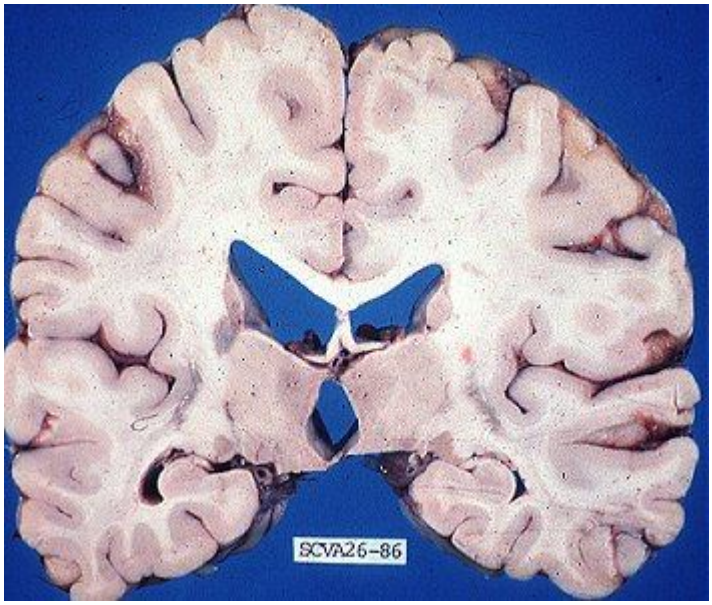


Figure 2. **Coronal section at the level of the thalamus and lateral geniculate bodies showing multifocal small plaques in the white matter of the periventricular and perithalamic regions.**

Low-density lesions in the white matter can often be seen on a contrast-enhanced CT scan, but MRI is a considerably more powerful technique for imaging areas of demyelination. However, the extent and severity of lesions on MRI may not correlate with the clinical syndrome (Osborn et al, 1990). Visual evoked responses are useful to document prior or concurrent optic neuritis, and peroneal somatosensory evoked responses can be used to document myelitis.

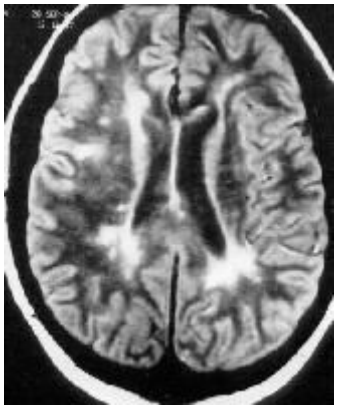


Figure 3. MS plaques are characteristically ovoid, abutting the ventricular borders in a confluent poorly demarcated pattern

Treatment. A course of ACTH or corticosteroids is recommended at the time of acute exacerbations. Prednisone is generally administered orally at a dosage of 2 mg/kg/day for I week and is then rapidly tapered and discontinued at the end of a month. Some believe that ACTH is superior to corticosteroids in adults with multiple sclerosis.

Aqueous ACTH, 80 units, is given intravenously over 8 hours in 5% dextrose and water each day for 3 days. Forty units of ACTH gel is then given intramuscularly every 12 hours for 7 days. Each injection is reduced by 5 units every 3 days. Improvement, when it occurs, is expected during the first 2 weeks.

- **Myoclonic Encephalopathy-Neuroblastoma Syndrome**
- **Pseudoataxia (Epileptic)**

- **Trauma**

Mild head injuries are common in children, especially toddlers. Recovery is always complete despite considerable parental concern. More serious head injuries, associated with loss of consciousness, seizures, and cerebral contusion, are less common but still account for several thousand deaths in children annually. Ataxia may follow head injuries, even mild ones. In most of these cases the ataxia is part of the so-called postconcussion syndrome, in which no structural derangement of the nervous system can be demonstrated. In others a cerebellar contusion or posterior fossa hematoma may be present.

Ataxia may also follow cervical injuries, especially during sports. These are usually caused by trauma to the vertebrobasilar artery.

- **Postconcussion Syndrome**

Clinical Features. Many adults complain of headache, dizziness, and mental changes following even a mild head injury. The frequency of such complaints is greater and the symptoms are more severe and long lasting when litigation is pending. Some of these symptoms also occur after head injury in children and probably represent a transitory derangement of cerebral function caused

by the trauma. Even mild head trauma can produce structural disturbances in the brain, which may explain the persistence of symptoms.

In infants and small children the most prominent postconcussive symptom is ataxia. This is not necessarily a typical cerebellar ataxia but may be only an unsteady gait. No limb dysmetria is present, and the remainder of the neurologic findings are normal.

In older children with postconcussive syndromes, headache and dizziness are as common as ataxia. The headache is usually described as low grade and constant, sometimes made worse by movements of the head. Gait is less disturbed, possibly because an older child better compensates for dizziness, but the sensation of unsteadiness is still described.

Diagnosis. An imaging study is necessary in many children with postconcussive symptoms to exclude the possibility of subdural hematoma.

Treatment. Ataxia usually clears completely within I month and always within 6 months. Decreased activity during this time is recommended. Usually no further treatment is required.

- **Vertebrobasilar Occlusion**

Trauma to the vertebrobasilar arteries is reported with chiropractic manipulation and sports injuries (Zimmerman et al, 1978). The vertebral arteries are encased in bony canals from C-2 to the foramen magnum. Sudden stretching of the arteries by hyperextension or hyperflexion of the neck causes endothelial injury and thrombosis.

Clinical Features. Symptoms are noted within minutes or hours of injury. Vertigo, nausea, and vomiting are the initial manifestations of brainstem ischemia. Occipital headache may be present as well. Ataxia is due to incoordination of the limbs on one side. It may be maximal at onset or progress over several days.

Examination demonstrates some combination of unilateral brainstem disturbances (diplopia, facial weakness) and ipsilateral cerebellar dysfunction.

Diagnosis. CT or MRI reveals a unilateral infarction in the cerebellar hemisphere. The lateral medulla may also be infarcted. The location of arterial thrombosis is visualized by arteriography.

Treatment. Many children recover completely in the months that follow injury. The value of anticoagulation has not been established.

- **Vascular lesions**
  - **Cerebellar Hemorrhage**

Spontaneous cerebellar hemorrhage in children, in the absence of a coagulopathy, is due to arteriovenous malformation, even though less than 10% of intracranial arteriovenous malformations in children are in the cerebellum. The two major features of cerebellar hemorrhage are ataxia and headache.

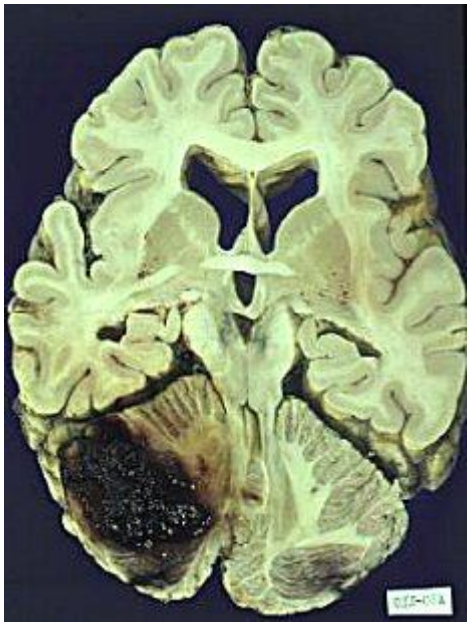
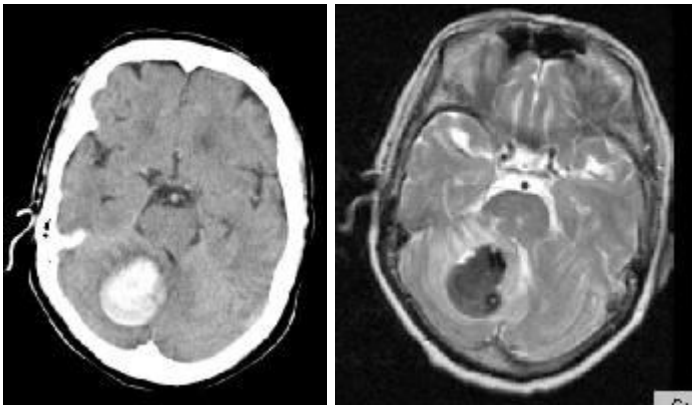


Figure 4. Acute cerebellar hemorrhage

Figure 5. A female with hypertension presented with acute-onset ataxia and confusion. Noncontrast CT exam of the head [left image] showed a large, right cerebellar hemorrhage, which was evacuated to relieve the mass effect on the brainstem and fourth ventricle. The cerebellar hemorrhage is seen hypointense on the T2 image due to Deoxyhemoglobin [right image].



- **Lupus Erythematosus**

Cerebellar disturbances occur in systemic lupus erythematosus (Sergent et al, 1975). The peak incidence of lupus erythematosus is in girls near the time of puberty.

Clinical Features. The major clinical features are fever, rash, arthritis or arthralgia, and cardiac abnormalities, including cardiomegaly, pericarditis, myocarditis, and congestive heart failure. Gastrointestinal bleeding, abnormal renal function, and cardiac disturbances indicate a poor prognosis for survival. Neurologic complications of lupus erythematosus ordinarily occur late in the course of disease, after the diagnosis is already established. The most common neurologic manifestations are seizures, personality changes, and chorea. However, cerebellar ataxia is sometimes noted as an isolated finding or in association with other neurologic manifestations.

Diagnosis. Systemic lupus erythematosus is an unlikely diagnosis in a previously healthy child with acute ataxia. When clinical symptoms and signs are compatible with the diagnosis, the demonstration of high concentrations of antinuclear antibody is confirmatory.

Treatment. Corticosteroids alone or in combination with cytotoxic agents are used to treat the underlying disease and its neurologic complications. Daily administration of high-dose cortico-steroids is recommended, although their benefit has not been established.

CHRONIC PROGRESSIVE ATAXIA

Brain tumor is always an initial consideration when progressive ataxia develops in children who were previously normal, especially if headache is present as well (Table 2). Congenital abnormalities that cause ataxia are frequently associated with some degree of mental deficiency. The onset of symptoms may occur during infancy or be delayed until adult life. With the exception of Friedreich ataxia, chronic ataxia is rarely hereditary. However, most cases are easily diagnosed and many are treatable. Failure to diagnose the underlying cause of chronic ataxia can have unfortunate consequences for the child.

- **Brain tumours**

Neuroectodermal tumors are the second most common malignancy of childhood and the most common solid tumor. Posterior fossa tumors are more common than supratentorial tumors between the ages of 1 and 8 years and account for approximately 50% of brain tumors in children of all ages (Schulte, 1984). The four major tumors of the posterior fossa are cerebellar astrocytoma, brainstem glioma, ependymoma, and medulloblastoma. Ataxia is a late manifestation of brainstem glioma; the initial features are disturbances of cranial nerve function. Although this discussion is limited to tumors of the posterior fossa, it is important to remember that supratentorial brain tumors may also cause ataxia. Twenty-two percent of children with supratentorial brain tumors have gait disturbances at the time of their first hospitalization, and 17% have "cerebellar signs" (Gjerris, 1978). Gait disturbances occur with equal frequency whether supratentorial tumors are in the midline or the hemispheres, whereas cerebellar signs are more common with midline tumors.

  - **Cerebellar Astrocytoma**

Cerebellar astrocytomas constitute 16% to 20% of brain tumors in children. Less than 20% are malignant. The tumor may be in the hemisphere, in the vermis, or in both hemisphere and vermis or may occupy the fourth ventricle (Tomita, 1983).

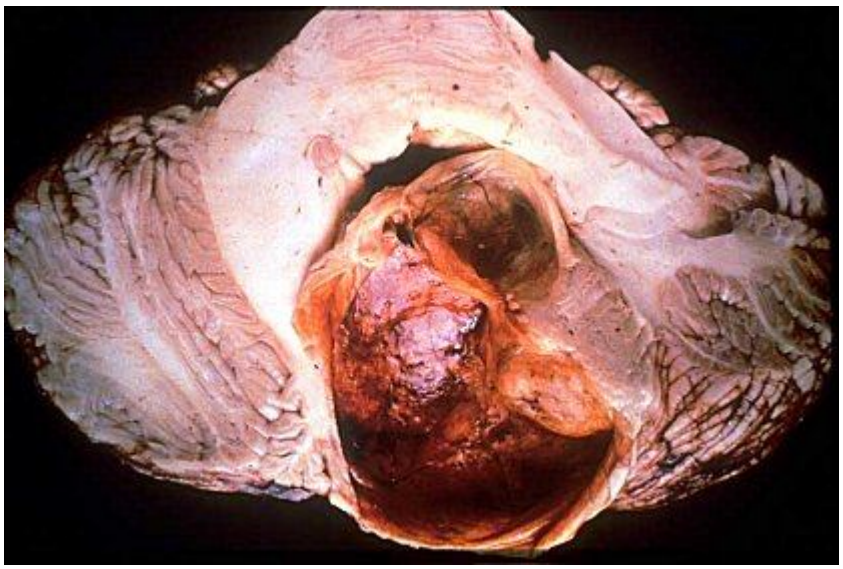


Figure 6. A pilocytic astrocytoma, notice the peripherally located hypercellular part (mural nodule) the multicystic appearance of the tumour

Clinical Features. Both sexes are affected equally. The onset of symptoms is usually after 3 years of age but may be as early as infancy. Headache is the most common initial complaint in school-age children, whereas unsteadiness of gait and vomiting are the initial symptoms in preschool children. Headache can be insidious and intermittent; only rarely is there typical morning

headache and vomiting. The first complaints of headache and nausea are usually attributed to a flulike illness. Only when symptoms persist is the possibility of increased intracranial pressure considered. In infants and small children symptoms of increased intracranial pressure are often relieved by the separation of cranial sutures. For this reason gait disturbances without headache or vomiting are the common initial sign of cerebellar astrocytoma in infants.

Papilledema is present in almost 83% of affected children at initial examination but is often absent in infants with separation of cranial sutures. Ataxia is present in 72%, dysmetria in 50%, and nystagmus in only 22% of these children.

Ataxia varies in severity from a wide-based lurching gait to a subtle alteration of gait observed only with tandem walking or quick turning. It is caused in part by the cerebellar location of the tumor and in part by hydrocephalus. When the tumor is in the cerebellar hemisphere, ipsilateral or bilateral dysmetria may be present. Other neurologic signs sometimes present in children with cerebellar astrocytoma include abducens palsy, multiple cranial nerve palsies, stiff neck, and head tilt.

Diagnosis. CT or MRI is suitable for diagnosis.

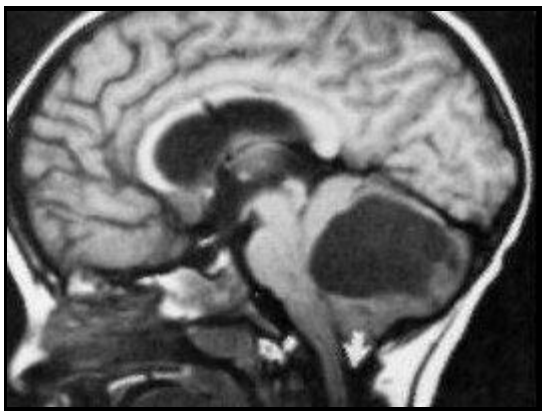


Figure 7. MRI image showing cerebellar pilocytic astrocytoma

Treatment. Children with life-threatening hydrocephalus should undergo a shunting procedure as the first step in treatment. The shunt relieves many of the symptoms and signs, including ataxia (Hendrick, 1983).

Corticosteroids are sufficient to relieve pressure in many children with less severe hydrocephalus.

An astrocytoma in the cerebellar hemisphere can be surgically extirpated. Such tumors are usually cystic, and removal of the mural nodule is curative. Deeper tumors that involve the floor of the fourth ventricle are rarely removed in toto. Local recurrence is common after partial resection. Repeat surgery may be curative in some cases, but postoperative radiation therapy appears to offer a better prognosis following partial resection. In one series the overall disease-free survival rates following either surgery alone or surgery and radiation therapy were 92% at 5 years and 88% at 25 years (Garcia et al, 1989). Chemotherapy is not currently recommended for low-grade cerebellar astrocytomas regardless of the degree of surgical resection.

High-grade cerebellar astrocytoma (glioblastoma) has rarely been reported in children. More than 30% of childhood patients have dissemination of tumor through the neuraxis (spinal cord drop metastases). Examination of cerebrospinal fluid for cytologic features and complete myelography are recommended following surgical resection in all patients with glioblastoma. If either result is abnormal, whole-axis radiation therapy is indicated.

- **Cerebellar Hemangioblastoma (von Hippel- Lindau Disease)**

Von Hippel-Lindau disease is a multisystem disorder transmitted by autosomal dominant inheritance (Neumann and Wiestler, 1991). The most prominent feature is hemangioblastomas of the cerebellum and retina (Maher et al, 1990). All children with cerebellar hemangioblastoma have von Hippel-Lindau disease. Among adults, 60% have isolated tumors and do not have the genetic defect. The expression of von Hippel-Lindau disease is variable even within a kindred. The most common manifestations are cerebellar and retinal hemangioblastoma (59%), renal carcinoma (28%), and pheochromocytoma (7%).

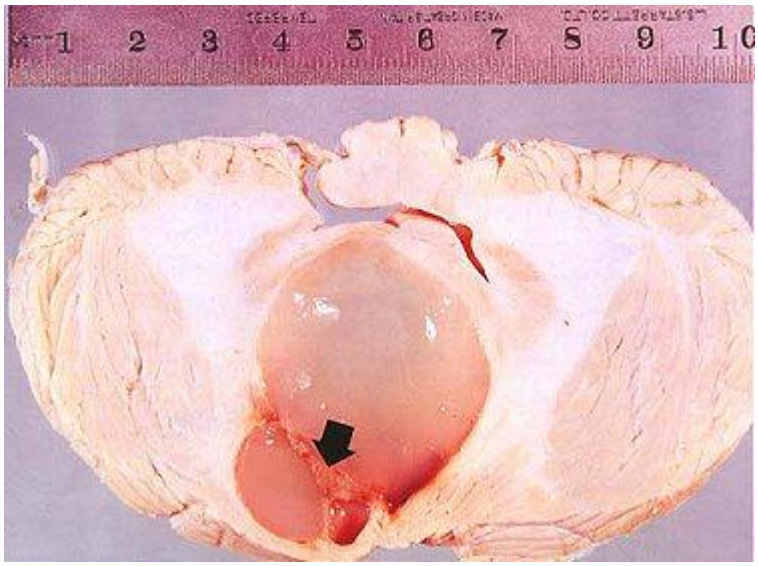


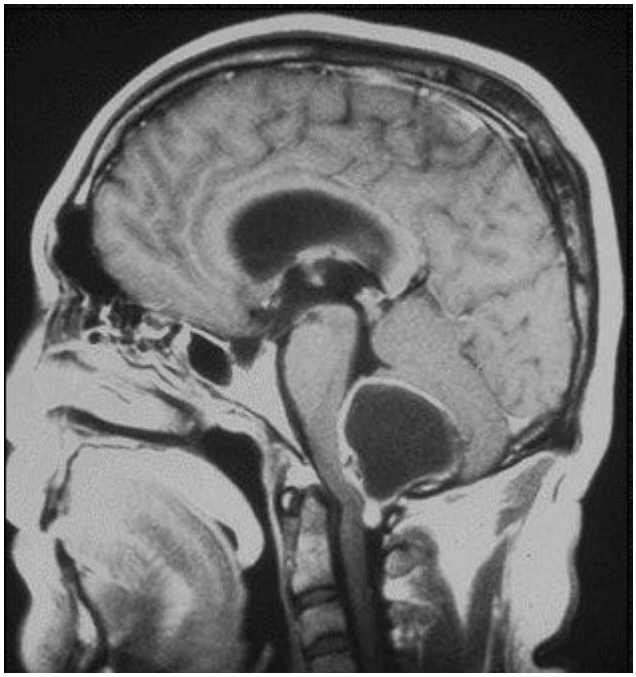
Figure 8. Hemangioblastoma: The tumor itself is composed of small triangular fragments of brownish tissue marked by the arrow. Notice the presence of three associated cysts.

Clinical Features. Mean age at onset of cerebellar hemangioblastoma in von Hippel-Lindau disease is 32 years; onset before 15 is unusual. The initial features are headache and ataxia. Retinal hemangioblastomas occur at a younger age and may cause visual impairment resulting from hemorrhage as early as the first decade. They may be multiple and bilateral and appear on ophthalmoscopic examination as a dilated artery leading from the disk to a peripheral tumor with an engorged vein.

Diagnosis. The diagnosis of von Hippel-Lindau disease is based on the presence of any of the following: more than one hemangioblastoma of the central nervous system; an isolated hemangioblastoma associated with a visceral cyst or renal carcinoma; or any known manifestation with a family history of the disease.

Gadolinium-enhanced MRI is useful for detecting tumors in the central nervous system (Filling-Katz et al, 1991). Visceral manifestations can be identified by abdominal CT scan and ultrasound.

Figure 9. MRI T1 postcontrast images showing cerebellar hemangioblastoma, notice the rim and



nodular enhancement.

Treatment. Children at risk for von Hippel- Lindau disease should be screened for retinal hemangioblastomas by indirect ophthalmoscopy every 5 years. Cryotherapy or photocoagulation of smaller lesions can lead to complete tumor regression without visual loss.

MRI should be performed in any child with ataxia and at 5-year intervals after 15 years of age in persons with genetic risk factors. Cerebellar hemangioblastoma should be treated surgically and can often be totally extirpated.

Visceral manifestations are uncommon in childhood, but adults must be screened with abdominal CT.

- **Ependymoma**

Posterior fossa ependymoma is derived from the cells that line the roof and floor of the fourth ventricle. These tumors can extend into both lateral recesses and grow out to the cerebellopontine angle. They account for 10% of primary brain tumors in children.

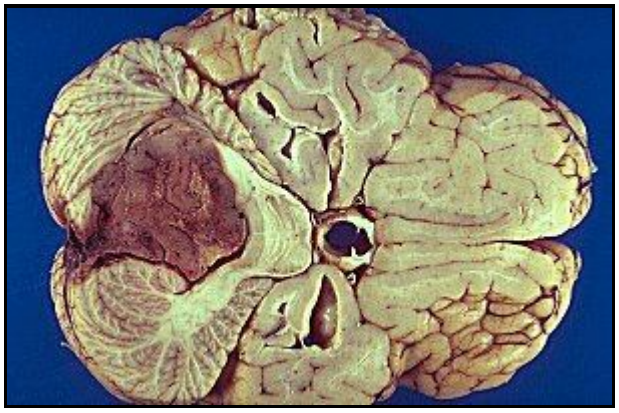


Figure 10. A 4th ventricular ependymoma compressing the brain stem and composed of the characteristic rosettes

Clinical Features. Ependymoma is primarily a tumor of young children; 50% become symptomatic before three years of age (Choux, 1983). Both sexes are affected equally.

Symptoms evolve more slowly in children with ependymoma than in those with medulloblastoma. Symptoms are commonly present for several months before medical consultation is sought. Symptoms for increased intracranial pressure are the first manifestation in 90% of patients. Disturbances of gait and coordination, neck pain, or cranial nerve dysfunction is the initial symptom in the remainder. Fifty percent of patients have ataxia, usually of the vermial type, and 33% have nystagmus. Head tilt or neck stiffness is present in one third of children and indicates extension of tumor into the cervical canal.

Although steady deterioration is expected, some children have an intermittent course. Transient episodes of headache and vomiting, ataxia, and even nuchal rigidity lasting for days or weeks are followed by periods of well-being. These intermittent symptoms are caused by transitory obstruction of the fourth ventricle or aqueduct by the tumor acting in a ball-valve fashion.

Diagnosis. CT and MRI are equally useful for diagnosis. The ventricular system is almost always markedly dilated. MRI better demonstrates the tumor's location in the fourth ventricle and its extraventricular extensions.

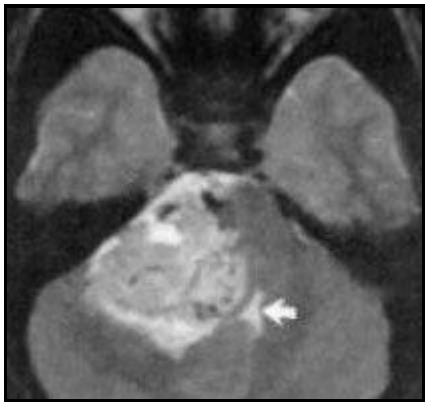


Figure 11. Ependymoma in a 7-year-old boy

Treatment. The goals of surgical therapy are to relieve the hydrocephalus and to remove as much tumor as possible without damaging the fourth ventricle. Postoperative irradiation to the posterior fossa, but not the neuraxis, is usually indicated. A postoperative mortality rate of approximately 30% is noted in several series. Five-year survival rates vary from 33% to 70%.

High-grade ependymomas and Ependymoblastomas are likely to seed the spinal subarachnoid space and require whole neuraxis irradiation. In addition, chemotherapeutic agents similar to those used for medulloblastoma should be administered.

- **Medulloblastoma**

Medulloblastoma is a primitive neuroectodermal tumor with the capacity to differentiate into neuronal and glial tissue. Most tumors are in the vermis or fourth ventricle with or without extension into the cerebellar hemispheres. Approximately 10% are in the hemisphere alone (Tomita, 1983).

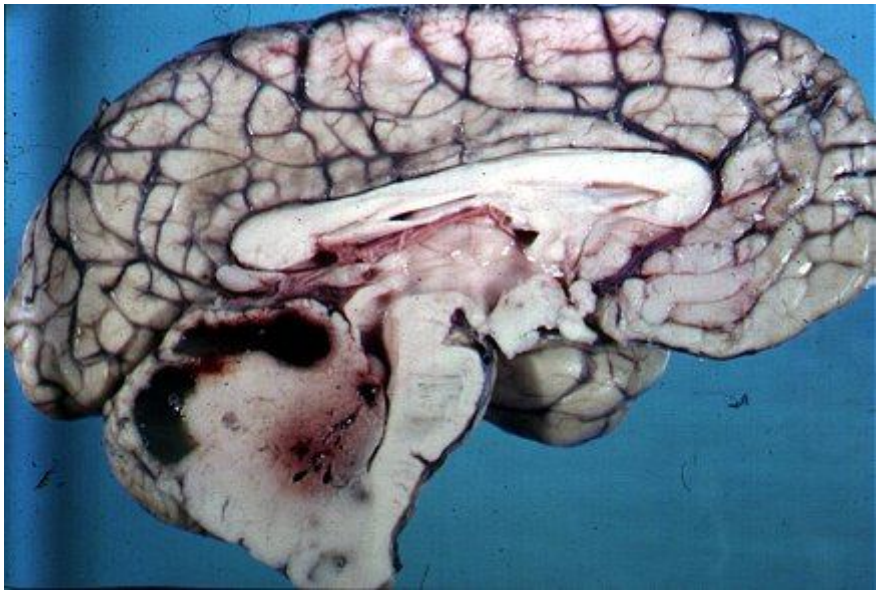


Figure 12. Medulloblastoma compressing the brain stem. Notice the hemorrhagic components.

Clinical Features. Most series indicate a male-to-female ratio of 3:2. Ninety percent of cases have their onset during the first decade and the remainder during the second decade. Medulloblastoma is the most COMMON primary brain tumor with onset of symptoms during infancy.

The tumor grows rapidly, and the interval between onset of symptoms and medical consultation is generally brief: 2 weeks in 25% of cases and less than a month in 50%. Vomiting is an initial symptom in 58% of children, headache in 40%, an unsteady gait in 20%, and torticollis or stiff neck in 10%. The predominance of vomiting, with or without headache, as an early symptom is probably caused when the tumor irritates the floor of the fourth ventricle. Gait disturbances are more common in young children and are characterized by refusal to stand or walk rather than by ataxia.

Two thirds of children have papilledema at the time of initial examination. Truncal ataxia and limb ataxia are equally common, and both may be present. Only 22% of children have nystagmus. Tendon reflexes are hyperactive when hydrocephalus is present and hypoactive when the tumor is causing primarily cerebellar dysfunction.

Diagnosis. Medulloblastoma is readily diagnosed with CT or MRI. The tumors are highly vascular and become enhanced when contrast medium is used.

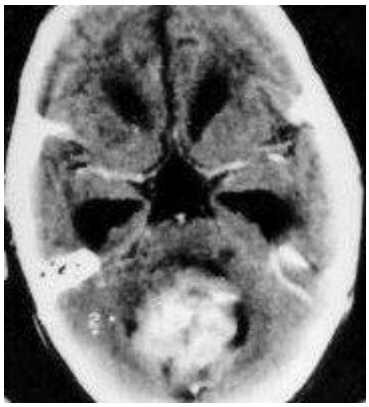


Figure 13. CT scan showing a medulloblastoma

Treatment. The prognosis for children with medulloblastoma is greatly improved by the combined use of surgical extirpation, radiation therapy, and chemotherapy. The role of surgery is to provide

histologic identification, debulk the tumor, and relieve obstruction of the fourth ventricle.

Children with medulloblastoma are divided into high- and low-risk groups for the purpose of designing therapy. The high-risk, or poor prognosis, group includes those with any evidence of tumor dissemination, more than 1.5 cm of residual tumor following initial surgery, tumors invading two structures or completely filling the fourth ventricle, or tumor filling the fourth ventricle and extending to the third ventricle or the cervical cord. Radiation therapy is necessary for children in both the high- and low-risk groups. Medulloblastoma is more radiosensitive than is glioma, and a lower total dose of radiation can be used (Tomita and McLone, 1986). Before radiation is initiated, a complete myelogram must be obtained to determine whether drop metastases are present. Areas with visible metastatic disease receive a larger radiation dose.

Children in the high-risk group are treated with chemotherapy as well as radiation. This combination has improved 5-year survival rates by more than 10%. Experimental protocols are being tested, and children with medulloblastoma should be referred to specialized centers for chemotherapy (Packer, 1990).

When the combined approaches of surgery, irradiation, and chemotherapy are used, the 5-year survival rate is 50% to 70%.

- **Congenital malformation**
    - **Basilar Impression**

Basilar impression is a disorder of the craniovertebral junction in which the odontoid process is displaced posteriorly and compresses the spinal cord or brainstem.

Clinical Features. The first symptoms are often head tilt, neck stiffness, and headache. The onset of symptoms is frequently precipitated by minor trauma to the head or neck. Examination reveals ataxia, nystagmus, and hyperreflexia (Teodori and Painter, 1984).

Diagnosis. CT demonstrates invagination of the odontoid process into the foramen magnum. MRI may be useful to delineate an associated Chiari malformation or syringobulbia.

Treatment. Surgical decompression of the foramen magnum usually relieves symptoms.

- **Cerebellar Malformations**
    - **Cerebellar Hemisphere Hypoplasia**

Congenital hypoplasia of the cerebellum occurs in humans as an autosomal recessive disease and can be experimentally induced in immature animals by cytotoxic drugs, irradiation, or viral infection.

- **Vermal Aplasia**

Aplasia of the vermis is relatively common and often associated with other cerebral malformations. All or part of the vermis may be missing, and when the vermis is incomplete, the caudal portion is usually lacking.

Clinical Features. Partial agenesis of the cerebellar vermis may be asymptomatic. These families

with dominantly inherited aplasia of the anterior vermis have been reported; whether the pattern is autosomal or X-linked dominant is unknown (Fenichel and Phillips, 1989). Symptoms are nonprogressive and vary from only mild gait ataxia and upbeating nystagmus to severe ataxia.

Complete agenesis causes titubation of the head and truncal ataxia. Vermal agenesis is frequently associated with other cerebral malformations, producing a constellation of symptoms and signs referable to neurologic dysfunction. Two such examples are the Dandy-Walker malformation and the Joubert syndrome (Appleton et al, 1989).

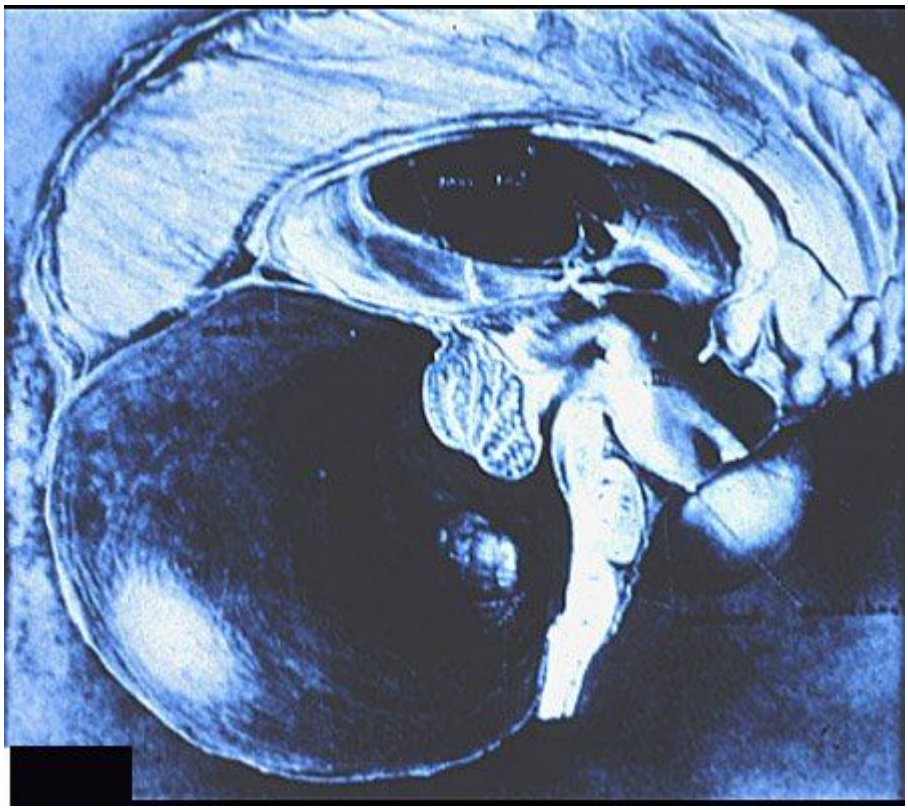


Figure 14. The Dandy-Walker syndrome is a complex malformation of posterior fossa structures. This may be associated with atresia of the foramina of Magendie and /or Luschka. According to one theory the failure of these foramina to open during embryonic development leads to enlargement of the fourth ventricle, with secondary compression of the cerebellum. The latter phenomenon results in failure of normal development of the cerebellum, accounting for the frequent small size of the cerebellum, as demonstrated in this slide. The large cyst in this slide is actually an enlargement of the fourth ventricle and not separate from it. The third ventricle and lateral ventricles are markedly enlarged secondarily

Cerebellar vermal agenesis is a constant feature of the Joubert syndrome, but several other cerebral malformations are usually present as well. More than one sibling in a family may be involved, but the parents are normal. The typical clinical manifestation in newborns and infants is periods of hyperpnea, usually about 120 breaths/ min and lasting for up to 16 seconds, alternating with episodes of apnea lasting up to 12 seconds. Abnormal, conjugate jerking eye movements are observed in half of infants. Most infants are hypotonic. Tendon reflexes may be normal or exaggerated. All patients are mentally retarded, and some are microcephalic. Several affected children have died unexpectedly, possibly from respiratory failure.

Diagnosis. CT or MRI shows agenesis of the vermis of the cerebellum with enlargement of the cisterna magna. Other cerebral malformations, such as agenesis of the corpus callosum, may be observed as well.

Treatment. No treatment is available.

- **Chiari Malformation**

The Chiari malformation is a displacement of the cerebellar tonsils into the upper cervical canal, sometimes accompanied by caudal dislocation of the hindbrain. Children with the Chiari malformation may have myelomeningocele as well. When the Chiari malformation is present without meningocele, the onset of symptoms is frequently delayed until adolescence or adult life.

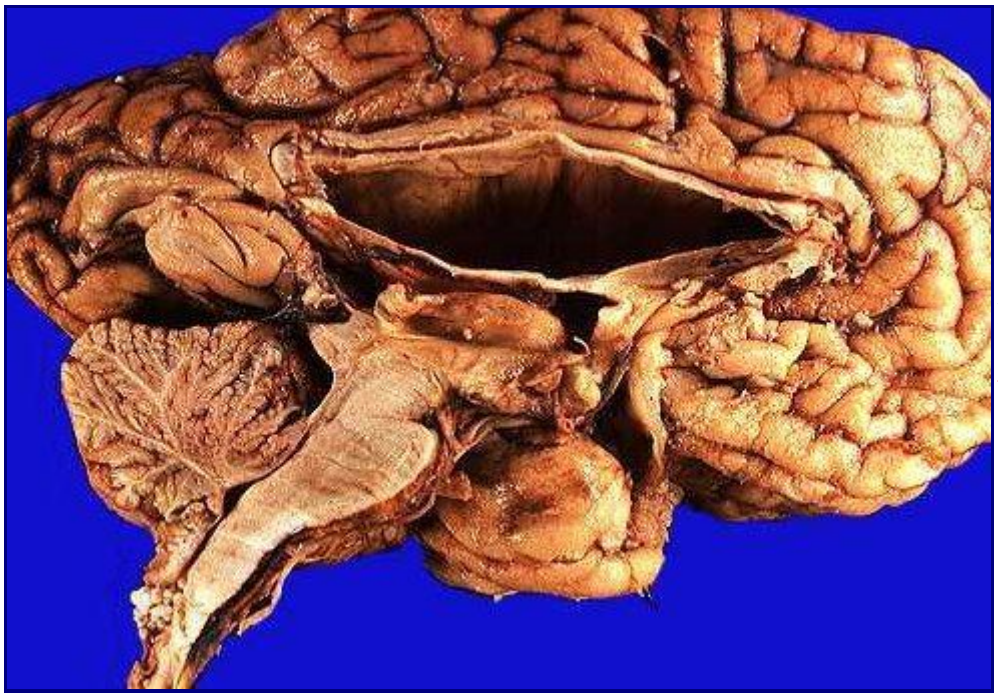


Figure 15. Arnold Chiari malformation associated with hydrocephalus

Clinical Features. Major clinical features are headache, head tilt, pain in the neck and shoulders, ataxia, and lower cranial nerve dysfunction (Levy et al, 1983). Physical signs vary among patients. Features found in approximately half of cases include weakness of the arms, hyperactive tendon reflexes in the legs, nystagmus, and ataxia.

Diagnosis. MRI provides the best visualization of posterior fossa structures. The distortion of the cerebellum and hindbrain is precisely identified.

Treatment. Surgical decompression of the foramen magnum to at least the C3 vertebra is recommended (Park et al, 1983). More than half of patients are significantly improved by surgery.

- **Hereditary ataxia**
  - **Autosomal Recessive**
    - **Friedreich Ataxia**

The term "Friedreich ataxia" has been used in a generic sense to describe all spinocerebellar degenerations. This usage is not helpful. Strict clinical criteria for Friedreich ataxia define a more homogeneous group of patients who have a predictable course (Harding, 1981; Stumpf, 1985). These criteria include autosomal recessive inheritance, onset of ataxia or scoliosis before 20 years of age, rapid early progression, and absence of ophthalmoplegia and dementia.

Clinical Features. Clinical features are similar in members of the same family. Heterozygotes have no manifestations of disease, and the presence of abnormal signs, such as pes cavus or scoliosis, in parents should suggest a dominantly inherited ataxia or Charcot-Marie-Tooth disease (Harding,

1981).

In the majority of cases the onset occurs between 2 and 16 years of age, but occasionally the symptoms begin earlier or later. The initial manifestation is ataxia or clumsiness of gait in 95% of cases and scoliosis in 5%. The course is one of steady deterioration; most patients are confined to a wheel- chair within 20 years of onset. Dysarthria develops in all patients. Disturbances of ocular motility occur in 32% of patients and deafness in 8%. Titubation of the head is present in only 4%. Symptoms of cerebellar dysfunction are more severe and more common in the arms than in the legs. Finger-nose ataxia and difficulty in performing rapid alternating movements develop in almost every patient. Only 28% of patients demonstrate the same symptoms in the legs, but spastic weakness is often present and may hide the cerebellar signs.

All tendon reflexes are absent in 75% of patients. In the other 25%, reflexes are obtained only at the biceps muscles. Children with a Friedreich- like syndrome but in whom tendon reflexes are retained at the arms and knees probably have a different genetic disorder (see discussion of Harding ataxia). Extensor plantar responses are present in 89%. Joint position sense and vibration sense are absent in the feet in 90% and in the hands in 27%. Light touch and pain sensations are impaired in less than 10% of patients.

Scoliosis develops in 79% and pes cavus in 55% of patients. The severity of the skeletal deformities varies and is usually mild. A cardiomyopathy characterized by dyspnea on exertion, palpitations, and angina develops in 40% of patients. Systolic ejection murmurs, heard best over the apex or left sternal edge, are relatively common.

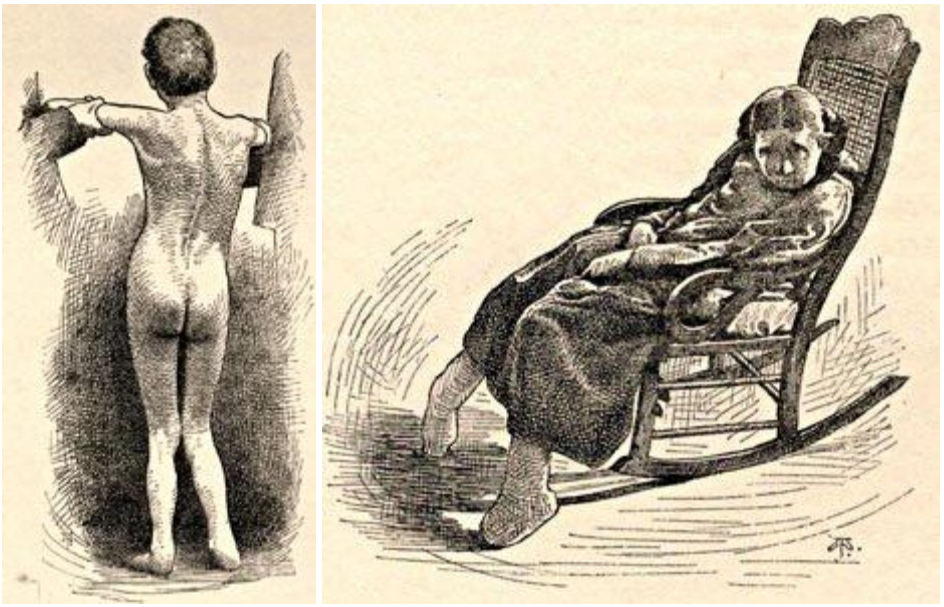


Figure 16. Friedreich Ataxia

Diabetes is present in 10% of patients and has its onset during the third decade. The diabetes tends to be severe, may be difficult to control with insulin, and can significantly contribute to death from the disease.

Diagnosis. The diagnosis relies primarily on the clinical features. Motor nerve conduction velocities in the arms and legs are slightly slower than normal. In contrast, sensory action potentials are either absent or markedly reduced in amplitude. Spinal somatosensory evoked responses are usually absent.

Common changes on the electrocardiogram (EKG) are a reduced amplitude of T waves and left or

right ventricular hypertrophy. Arrhythmias and conduction defects are uncommon.

Treatment. The underlying disturbance is not curable, but symptomatic treatment is available. Severe scoliosis should be prevented by orthopedic intervention. The development of cardiomyopathy must be monitored by regular EKG and chest radiographs to determine heart size. Chest pain on exertion responds to propranolol, and congestive heart failure responds to digitalis. Patients should be checked for diabetes and should be given insulin when necessary.

Table 3. Metabolic Screening in Progressive Ataxias

Disease	Abnormality
Blood	
Adrenoleukodystrophy	Very-long-chain fatty acids
Ataxia-telangiectasia	IgA, IgE, alpha-fetoprotein
Abetalipoproteinemia	Lipoproteins, cholesterol
Hypobetalipoproteinemia	Lipoproteins, cholesterol
Mitochondrial disorders	Lactate, glucose-lactate tolerance
Sulfatide lipidoses	Arylsulfatase A
Urine	
Hartnup disease	Amino acids
Maple syrup urine disease	Amino acids
Fibroblasts	
GM, gangliosidosis	Hexosaminidase
Refsum disease	Phytanic acid
Carnitine Acetyltransferase deficiency	Carnitine Acetyltransferase
Bone Marrow	
Neurovisceral storage	Sea-blue histiocytes

- **X-Linked Inheritance**

The infantile form of adrenoleukodystrophy and Leber optic neuropathy may initially be manifested as ataxia. Adrenoleukodystrophy may more closely mimic a spinocerebellar degeneration and should be considered in any family with only males affected (Kobayashi et al, 1986). Leber optic neuropathy is readily distinguished from other cerebellar degenerations because other family members have characteristic ophthalmologic features.

PHARMACOLOGICAL MANAGEMENT OF CEREBELLAR DEFICITS

The pharmacologic therapies for cerebellar deficits have met with limited success (Table 4). This is to be expected because many of these trials involve a heterogeneous collection of diseases that are seen with cerebellar deficits as a common clinical endpoint. Pharmacopathology, and, therefore, therapeutic efficacy of any one agent, may vary greatly. Even attempts to run trials on specific primary degenerative diseases may have this same flaw given their poor nosology. But these data are not to be ignored when faced with the cerebellar patient in the clinical setting.

Responders to these various drugs cannot be predicted, so side effects and usefulness must be weighed for each patient.

TABLE 4. Selected Drug Trials for Cerebellar Deficits.

Category	Compound	Result
Anticonvulsants	Carbamazepine	Moderate improvement in cerebellar tremor.
	Clonazepam	Moderate-to-good effect for cerebellar tremor.
	Vigabatrin	Mild improvement in ataxia in small minority of patients with degenerative disorders.
Cholinergic agents	Physostigmine	Mild improvement in global functioning in the hereditary ataxias.
	Choline	Moderate-to-good response in global functioning in small minority of patients with degenerative disorders.
	Lecithin	Moderate improvement in global functioning in Friedreich's ataxia, Less successful in other degenerative disorders.
Other	Propranolol	No effect on cerebellar tremor.
	lsoniazid	Conflicting results for cerebellar tremor, none-to-moderate improvement.
	5-Hydroxytryptophan	Moderate-to-good response for cerebellar deficits, especially gait disorders. L-isomer with peripheral decarboxylase inhibitor works best.
	Thyrotropin releasing	Moderate-to-good response for hormone generalized cerebellar deficits in degenerative disorders.

The concept in drug treatment for cerebellar deficits, as in movement disorders. primarily centers around adjusting known neurotransmitters. However, these approaches do not give clear, consistent results. Take the example for GABA, an inhibitory amino acid transmitter that is present in the cerebellum and possibly used as a transmitter by several cell types, most notably the Purkinje cells. Therapeutic effects Of clonazepam and isoniazid are thought to be because of their

property as GABA agonists. But the use of vigabatrin and baclofen,. powerful centrally acting GABA agonists, have met with, at best, poor results. This lack of consistency may again reflect the biochemical heterogeneity of cerebellar deficits, or reflect the fact that simply adjusting neurotransmitters, in the classic sense, is not the issue. Some of the drug therapies appear to be used more as neuromodulators than as classic neurotransmitters. In contrast to classic neurotransmitters, neuromodulators have a slow and gradual onset in reaching their therapeutic effect, and this response may linger up to several weeks after they are stopped. Such an effect is seen with lecithin, choline, and 5- hydroxytryptophan. It is unclear whether neuromodulation is occurring directly at the level of the cerebellum or whether afferent and efferent cerebellar pathways are responsible.

Drug treatment of other neural systems involvement in the cerebellar patient should be addressed. For example, associated movement disorders in the primary spinocerebellar degenerations have included parkinsonian features, chorea, and myoclonus. These have been shown to respond, respectively, to L-dopa, baclofen, and trihexyphenidyl.

References

1. **Agamanolis DP, Potter JL, Naito HK, et al: Lipoprotein disorder, cirrhosis and olivopontocerebellar degeneration in two siblings. Neurology 36:674, 1986.**

2. **Aicardi J, Bartosa C, Andermann E, et al: Ataxia-ocular motor apraxia: A syndrome mimicking ataxia-telangiectasia. Ann Neurol 24:497, 1988.**

3. **Al-Din AN, Anderson M, Bickerstaff ER, et al: Brainstem encephalitis and the syndrome of Miller Fisher: A clinical study. Brain 105:481, 1982.**

4. **Appleton RE, Chitayat D, Jan JE, et al: Joubert's syndrome associated with congenital ocular fibrosis and histidinemia. Arch Neurol 46:579, 1989.**

5. **Asbury AK: Diagnostic considerations in Guillain Bare syndrome. Ann NeuTol 9:1, 1981.**

6. **Ashwal S, Thrasher TV, Rice DR, et al: A new form of sea- blue histiocytosis associated with progressive anterior horn cell and axonal degeneration. Ann Neurol 16:184, 1984.**

7. **Baloh RW, Winder A: Acetazolamide-responsive vestibulocerebellar syndrome: Clinical and oculographic features. Neurology 41:429, 1991.**

8. **Bejar JM, Ziegler DK: Onset of multiple sclerosis in a 24- month-old child. Arch Neurol 41:881, 1984.**

9. **Bennett HS, Selman JE, Rapin 1, et at: Nonconvulsive epileptiform activity appearing as ataxia. AJDC 136:30, 1982.**

10. **Boel M, Casaer P: Familial periodic ataxia responsive to flunarizine. Neuropediatrics 19:218, 1988.**

11. **Bolthauser E, Deonna A, Hirl HR: Myocionic encephalopathy of infants or "dancing eyes syndrome." Helv Paediatr Acta 34:119, 1979.**

12. **Boutin B, Esquivel E, Mayer M, et at: Multiple sclerosis in children: Report of clinical and paraclinical features of 19 cases. Neuropediatrics 19:118, 1988.**

13. **Bye AME, Kendall B, Wilson J: Multiple sclerosis in childhood: A new look. Dev Med Child Neurol 27:215, 1985.**

14. **Choux M: Ependymomas in the posterior fossa of children. In Amador LV, ed: Brain Tumors in the Young. Charles C Thomas, Springfield, III, 1983, p 526.**

15. **Danner DJ, Elsas LJ: Disorders of branched chain amino acid metabolism. In Scriver CR, Beaudet AL, Sly WS, et al, eds: The Metabolic Basis of Metabolic Disorders, 6th edition. New York, McGraw-Hill, 1989, p 67 1.**

16. **DiDonato S, Rimoldi M, Moise A, et al: Fatal ataxic encephalopathy and carnitine Acetyltransferase deficiency: A functional defect of pyruvate oxidation? Neurology 29:1578, 1979.**

17. **Evans OB: Episodic weakness in pyruvate decarboxylase deficiency. J Pediatr 105:961, 1984.**

18. **Ewout R, Brunt P, van Weerden TW: Familial paroxysmal kinesiogenic ataxia and continuous myokymia. Brain 113:1361, 1990.**

19. **Farlow MR, DeMyer W, Dlouhy SR, et al: X-linked recessive Inheritance of ataxia and adult-onset dementia: Clinical features and preliminary linkage analysis. Neurology 37:602, 1987.**

20. **Fariner TW, Wingfield MS, Lynch SA, et al: Ataxia, chorea, seizures, and dementia. Arch Neurol 46:774, 1989.**

21. **Farris BK, Smith JL, Ayyar R: Neuro-ophthalmologic findings in vestibulocerebellar ataxia. Arch Neurol 43:1050, 1986.**

22. **Fieit H, Kirkpatrick J, Van Woert MH, et al: Myoclonus, ataxia, and hypoventilation: Response to L-5-hydroxytryptophan. Neurology 33:109, 1983.**

23. **Fenichel GM: Migraine as a cause of benign paroxysmal vertigo in childhood. J Pediatr 71:114, 1967.**

24. **F,enichel GM, Phillips JA: Familial aplasia of the cerebellar vermis: Possible X-linked dominant inheritance. Arch Neurol 46:582, 1989.**

25. **Filla A, De Michele G, Cavalcanti F, et al: Clinical and genetic heterogeneity in early onset cerebellar ataxia with retained tendon reflexes. J Neurol Neurosurg Psychiatry 53:667, 1990.**

26. **Filling-Katz MR, Choyke PL, Oldfield E, et al: Central nervous system involvement in Von Hippel-Lindau disease. Neurology 41:41, 1991.**

27. **Fitzsimons RB, CHfton-Bligh P, Wolfenden WH: Mitochondrial myopathy and lactic acidemia with myoclonic epilepsy.- ataxia and hypothalamic infertility: A variant of Ramsay- Hunt syndrome? J Neurol Neurosurg Psychiatry 44:79, 198 1.**

28. **Fowler HL: Machado-Joseph-Azorean disease: A ten-year study. Arch Neurol 41:921, 1984.**

29. **Garcia DM, Latifi HR, Simpson JR. et al: Astrocytomas of the cerebellum in children. J Neurosurg 71:661, 1989.**

30. **Gartner JC, Bergman I, Malatack J, et &I: Progression of neurovisceral storage disease with supranuclear ophthalmoplegia following ordiotopic liver amplantation. Pediatrics 77:104, 1986.**

31. **Gatti RA, B(der E, Vinters HV, et al: Ataxia-telangiectasia: An interdisciplinary approach to pathogenesis. Medicine 70:99, 1991.**

32. **Gjerris F: Clinical aspects and long-term prognosis in supratentorial tumors of infancy and childhood. Acta Neurol Scand 57:445, 1978.**

33. **Graff-Radford NR; A recessively inherited ataxia with episodes of dystonia. J Neurol Neurosurg Psychiatry 49:591, 1986.**

34. **Haltia T, Palo J, Haltia M, et al: Juvenile metachromatic leukodystrophy: Clinical, biochemical, and neuropathologic studies in nine new cases. Arch Neurol 37:42, 1980.**

35. **Harding AE: Friedreich's ataxia: A clinical and genetic study of 90 families with an analysis of early diagnostic criteria and intrafamilial clustering of clinical features. Brain 104:589, 1981a.**

36. **Harding AE: Early onset cerebellar ataxia with retained tendon reflexes: Clinical and genetic study of a disorder distinct from Friedreich ataxia. J Neurol Neurosurg Psychiatry 44:503, 1981b.**

37. **Hegele RA, Angel A: Arrest of neutopathy and myopathy in abetalipoproteinemia with high-dose vitamin E therapy. Can Med Assoc J 132:41, 1985.**

38. **Hendrick EB: Medulloblastomas, astrocytomas, and sarcomas of the posterior fossa. In Amador LV, ed: Brain Tumors in the Young. Charles C Thomas, Springfield, 111, 1983, p 498.**

39. **Johnson WO: The clinical spectrum of hexosaminidase deficiency diseases. Neurology 31:1453, 1981.**

40. **Kobayashi T, Noda S, Umezaki H, et al: Familial spinocerrbellar degeneration as an expression of adrenoleukodystrophy. J Neurol Neurosurg Psychiatry 49:1438, 1986.**

41. **Lapkin ML, Golden GS: Basilar artery migraine. AJDC 132:278, 1978.**

42. **Levy HL: Hartnup disorder. In Scriver CR, Beaudet AL, Sly WS, et al, eds: The Metabolic Basis of Inherited Disease, 6th edition. McGraw-Hill, New York, 1989, P. 2515.**

43. **Levy WJ, Mason L, Hahn JF: Chiari malformation presenting in adults: A surgical experience in 127 cases. Neurosurgery 12:377, 1983.**

44. **Lima L, Coutinho P: Clinical criteria for diagnosis of Machado- Joseph disease: Report of a**

non-Azorean Portuguese family. Neurology 30:319, 1980.

45. **Livingstone IR, Gardner-Medwin D, Pennington RJT: Familial intermittent ataxia with possible X-linked recessive inheritance. J Neurol Sci 64:89, 1984.**

46. **MacFaul R, Cavanagh N, Lake BD, et al: Metachromatic leukodystrophy: Review of 38 cases. Arch Dis Child 3:168, 1982.**

47. **Maher ER, Yates JRW, Harries R, et al: Clinical features and natural history of von Hippel-Lindau disease. Q J Med 77:1151, 1990.**

48. **Marsdcn CD, Harding AE, Obesio JA, et al: Progressive myoclonic ataxia (the Ramsay Hunt syndrome). Arch Neurol 47:1121, 1990.**

49. **Meienberg 0, Ryffel R: Supranuclear eye movement disorders in Fisher's syndrome of ophthalmoplegia, ataxia, and areflexia: Report of a case and literature review. Arch Neurol 40:402, 1983.**

50. **Neumann HPH, Wiestier OT: Clustering of features of von Hippel-Lindau syndrome: Evidence for a complex genetic locus. Lancet 337:1052, 1991.**

51. **Nino HE, Noreen HJ, Dubey DP, et al: A family with hereditary ataxia: HLA typing. Neurology 30:12, 1980.**

52. **Osborn AG, Harnsberger HR, Smoker WRK, et al: Multiple sclerosis in adolescents: CT and MR findings. AJNR 11:489, 1990.**

53. **Packer RJ: Chemotherapy for medulloblastoma/primitive Neuroectodermal tumors of the posterior fossa. Ann Neurol 28:823, 1990.**

54. **Park TS, Hoffman HJ, Hendrick EB, et al: Experience with surgical decompression of the Arnold-Chiari malformation in young infants with myelomeningocele. Neurosurgery 13:147, 1983.**

55. **Pueschel SM, Bresnan MJ. Shih VE, et al: Thiamine-responsive intermittent branched chain ketoaciduria. J Pediatr 94:629, 1979.**

56. **Samat HB, Alcala H: Human cerebellar hypoplasia: A syndrome of diverse causes. Arch Neurol 37:300, 1980.**

57. **Schulte FJ: Intracranial tumors in childhood-concepts of treatment and prognosis. Neuropediatrie 15:3, 1984.**

58. **Scully RE, Mark EJ, McNeely BU: Case records of the Massachusetts General Hospital. N Engl J Med 315:1143, 1986.**

59. **Sergent JS, Lockshin MD, Klempner MS, et al: Central nervous system disease in systemic lupus erythematosus. Am J Med 58:644, 1975.**

60. **Somerville ER, Olanow CW: Valproic acid: Treatment of myoclonus in dyssynergia cerebellaris myoclonica. Arch Neurol 39:527, 1982.**

61. **Stumpf DA: The inherited ataxias. Pediatr Neurol 1: 129, 1985.**

62. **Takahashi H, Ohama E, Naito H, et al: Hereditary dentatorubral-pallidoluysian atrophy: Clinical and pathological variants in a family. Neurology 38:1065, 1988.**

63. **Teodori JB, Painter MJ: Basilar impression in children. Pediatrics 74:1097, 1984.**

64. **Tomita T: Statistical analysis of symptoms and signs in cerebellar astrocytoma and medulloblastoma. In Amador LV, ed: Brain tumors in the Young, Charles C Thomas, Springfield, IU, 1983, p 514.**

65. **Tomita T, McLone DG: Medulloblastoma in childhood: Results of radical resection and low-dose neuraxis radiation therapy. J Neurosurg 64:238, 1986.**

66. **Tuchman M, Morris CL, Ramnaraine ML, et al: Value of random urinary homovanillic acid and vanillylmandelic acid levels in diagnosis and management of patients with neuroblastoma. Pediatrics 75:324, 1985.**

67. **Vighetto A, Froment IC, Trillet M, et al: Magnetic resonance imaging in familial paroxysmal ataxia. Arch Neurol 45:547, 1988.**

68. **Waldmann TA, Misiti 1, Nelson DL, et al: Ataxia-telangiectasia: A multisystem hereditary disease with immunodeficiency, impaired organ maturation, X-ray hypersensitivity, and a high incidence of neoplasia. Ann Intem Mod 99:367, 1983.**

69. **Walker PD, Blitzer MG, Shapira E: Marinesco-SjVtn syndrome: Evidence for a lysosomal storage disorder. Neurology 35:415, 1985.**

70. **Wichman A, Buchthal F, Pezeshkpour GH, et al: Peripheral neuropathy in abetalipoproteinemia. Neurology 35:1279, 1985.**

71. **Wiliner JP, Grabowski GA, Gordon RE, et al: Chronic GM, gangliosidosis masquerading as atypical Friedreich ataxia: Clinical, morphologic, and biochemical studies of nine cases. Neurology 31:787, 1981.**

72. **Zasorin NL, Baloh RW, Myers LB: Acetazolamide-responsive episodic ataxia syndrome. Neurology 33:1212, 1983.**

73. **Zimmerman AW, Kumar AJ, Gadoth N, et al: Traumatic vertebrobasilar occlusive disease in childhood. Neurology 28:185, 1978.**

74. **Zoghbi HY, Pollack MS, Lyons LA, et al: Spinocerebellar ataxia: Variable age of onset and linkage to human leukocyte antigen in a large kindred. Ann Neurol 23:580, 1988.**

The author,

Professor Yasser Metwally

Professor of neurology, Ain Shams university, Cairo, Egypt

Visit my web site at: www.yassermetwally.com