Cerebellar Disorders

Neuroanatomy

The cerebellum can be divided into central structures (lingula, vermis and flocculonodular lobe) and the cerebellar hemispheres. Main inputs come from frontopontocerebellar connections (contralateral) from above, and spinocerebellar tracts from below ( proprioception) producing primarily ipsilateral signs.

Midline lesions can produce severe gait and truncal ataxia. As they extend they can also give fourth cranial nerve lesions and severe ipsilateral arm tremor, marked nystagmus, vertigo and vomiting, and can block CSF flow (obstructive hydrocephalus).

Cerebellar hemisphere lesions can produce classic ipsilateral limb ataxia (intention tremor, past pointing and mild hypotonia). Limb rebound can be demonstrated by gently pushing down on outstretched arms and then suddenly releasing, causing the arm on the affected side suddenly to fly upwards. Lateral lesions tend to produce more subtle nystagmus (maximal looking towards side of lesion).

Recent studies have also implicated the cerebellum in cognition and emotion. It has been considered that cerebellar dysfunction may contribute to non-motor conditions such as autism spectrum disorders.\[1\]

Note: lesions in the frontal lobe can produce 'pseudocerebellar signs' because of the way the frontal lobe influences the cerebellum and basal ganglia.

Aetiology\[2\]

- Vascular: stroke or transient ischaemic attack (TIA):
  - Usually with other brainstem features.
  - Infarction of the posterior inferior cerebellar artery causes lateral medullary syndrome (Wallenberg's syndrome) with hemiataxia, vertigo, dysarthria, ptosis and miosis

- Space-occupying: enlarging masses in the cerebellum may obstruct CSF flow, causing hydrocephalus and raised intracranial pressure. Coning of the cerebellar tonsils can occur rapidly (within hours), causing respiratory arrest.
  - Hydrocephalus.
  - Posterior fossa tumours or abscess.

- Nutritional:
  - Thiamine deficiency - Wernicke's encephalopathy (triad of acute confusion, ataxia and ophthalmoplegia); requires urgent thiamine treatment.
  - Vitamin E deficiency (including a genetic form).
  - Gluten sensitivity (gluten ataxia):
    - Neurological dysfunction can be the only manifestation of coeliac disease and, in this situation, typically presents as cerebellar ataxia, ± peripheral neuropathy
    - Intestinal symptoms and histological changes may be absent
    - The neurological features may reverse with a gluten-free diet.

- Zinc deficiency (rarely).

- Infections:
  - Bacterial: meningo-encephalitis or intracranial abscess.
  - Viral: acute infections (eg, varicella); chronic infections - eg, human immunodeficiency virus (HIV); post-viral syndromes (eg, post-infective cerebellar syndrome in childhood).
  - Parasitic infections (eg, toxoplasma, falciparum malaria, Lyme disease).
  - Prions: Creutzfeldt-Jakob disease (CJD), kuru.

- Toxins: alcohol, mercury, other heavy metals, solvents, carbon monoxide poisoning.
- Drugs: barbiturates, phenytoin, piperazine, antineoplastic drugs, deferiprone.\[4\]
- Drug overdose - eg, accidental temazepam overdose in children.
- Trauma.
- Multiple sclerosis (MS).
- Paraneoplastic cerebellar degeneration:
  - This is cerebellar disease occurring with cancer, but not due to brain secondaries; it may be related to antibodies.
  - It can occur with any cancer but most commonly with lung, gynaecological or breast cancer and Hodgkin's lymphoma.
Genetic: there are a number of inherited cerebellar ataxias:
- Many of these present in adulthood.
- Examples are Friedreich's ataxia (the most common) and ataxia telangiectasia.

Metabolic and endocrine:
- Cerebral oedema of chronic hypoxia.
- Wilson's disease (rare).
- Hypothyroidism (rarely).
- Inherited metabolic disorders - eg, Leigh's disease and the mitochondrial disorders

Congenital:
- Developmental anomalies - eg, cerebellar hypoplasia, Dandy-Walker syndrome, Arnold-Chiari malformation.
- Cerebral palsy.

There are various other uncommon neurological or metabolic diseases which may involve the cerebellum.
- Idiopathic cerebellar ataxia - a diagnosis of exclusion.

Presentation
As the cerebellum is associated with motor control, lesions produce a range of movement disorders (ataxias). These can be differentiated by their time course. Lesions of the midline vermis of the cerebellum cause truncal ataxia, while lesions of the cerebellar hemispheres cause limb ataxia of the ipsilateral side. Ataxia can be particularly difficult to diagnose in children.

Gait ataxia
Patients will tend to stand with feet well apart and are often frightened to stand. Patients tend to reel to the side of a unilateral lesion, or from side to side if central or bilateral (even if supported). Walking along a line of the floor demonstrates minor degrees of gait ataxia.

Truncal ataxia
Patients can't sit or stand unsupported and tend to fall backwards. It is caused by a midline cerebellar lesion, or may be a feature of post-chickenpox cerebellar syndrome. Truncal tremor may be evident - constant jerking of the trunk and head.

Limb ataxia
Lesions of the cerebellar hemisphere cause ipsilateral signs. The outstretched arm tends to be held hyperpronated at rest and at a slightly higher level than the unaffected side (Riddoch's sign), and rebounds upwards if gently pressed downwards and then suddenly released by the examiner. Finger-nose and heel-knee-shin tests will demonstrate even mild limb ataxia, with terminal intention tremor and dysmetria (past pointing).

Acute-onset ataxia
Either due to cerebellar haemorrhage or infarction. Haemorrhage presents with occipital headache, vertigo, vomiting and altered consciousness.

Subacute ataxia
May occur from:
- Viral infection - children aged 2-10 years; presents with pyrexia, limb and gait ataxia, dysarthria appearing over hours or days; takes up to six months for full recovery.
- Post-infectious encephalomyelitis - commonly related to varicella infection but other organisms may be involved.
- Other causes include - hydrocephalus, posterior fossa tumours, abscesses, parasitic infections and various toxins.

Episodic ataxias
These are episodes of ataxia lasting minutes to hours. May appear bizarre and may be misdiagnosed as being of hysterical origin. There are various causes:
- Drugs.
- MS.
- Transient vertebrobasilar ischaemic attacks.
- Foramen magnum compression.
- Inherited periodic ataxia, dysarthria, nystagmus and vertigo.
- Intermittent obstruction of the ventricular system, of which there are two types:
  - Brief attacks which may benefit from acetazolamide or phenytoin and the patient is usually well between attacks.
  - More prolonged attacks which are often associated with nausea, vertigo and vomiting. More severe in childhood with drowsiness, headache and fever and interictal nystagmus; slow deterioration in the ataxia and responds to acetazolamide (screen for metabolic disorder).

Chronic progressive ataxias
- Commonly caused by chronic alcohol abuse associated with malnutrition.
- May improve with thiamine.
• May also occur with other deficiencies, including zinc and vitamin E.
• Other causes include:
  • Ingestion of drugs - especially anticonvulsants, particularly phenytoin (may reverse once the drug is stopped).
  • Solvent abuse.
  • Heavy metals.
  • Structural lesions.
  • Paraneoplastic cerebellar degeneration associated with carcinomas of the lung or ovaries.
  • CJD (rare).

Other signs

Cerebellar dysarthria
Cerebellar disease can produce a spluttering staccato speech. Scanning dysarthria - jerky and explosive speech with separated syllables may be demonstrated by asking the patient to repeat "baby hippopotamus".

Writing
This may be larger than normal (contrast with micrographia of Parkinson's disease).

Rapid alternating movements
Cerebellar lesions produce inaccuracies in rapidly repeated movements (dysdiadochokinesia). This is demonstrated by getting the patient to tap the back of his/her own hand repeatedly with the other hand, or to tap his/her foot on the floor.

Tremor
Cerebellar lesions can produce unilateral or bilateral intention tremor, or a truncal tremor.

Nausea and vomiting
Cerebellar lesions can produce nausea and/or vomiting. Sudden vomiting (without warning) after a positional change, without preceding nausea, is suggestive of a posterior fossa lesion. There may be other signs secondary to obstructive hydrocephalus.

Cerebellar cognitive affective syndrome
The cerebellar cognitive affective syndrome includes impairments in decision-making, visual-spatial, and linguistic abilities, with affective disturbance ranging from emotional blunting and depression, to disinhibition and psychotic features.

Examination
• Check eye movement - looking for ophthalmoplegia or nystagmus.
• Check fundi for papilloedema.
• Get the patient to stick his/her tongue out and move it from side to side (movement slowed).
• Ask the patient to repeat "baby hippopotamus" - look for dysarthria and abnormal speech rhythm and syllable emphasis.
• Examine arms for limb ataxia (see above): rebound of outstretched arms, finger-nose test for past pointing, check for dysdiadochokinesia.
• Examine leg co-ordination with heel-shin test.
• Check limb power, tone and reflexes - cerebellar disorders may produce mild hypotonia and hyporeflexia.
• Ask the patient to sit up with arms crossed - looking for truncal ataxia.
• Ask the patient to walk heel-to-toe (to elicit any gait ataxia).
• If there are unilateral signs - check V, VII, and VIII (cerebellopontine angle pathology).

Cerebellar disorders in infants
Initially, these present with nonspecific motor development problems; nystagmus, incoordination and truncal ataxia on attempting to sit then later develop. Causes of cerebellar dysfunction in infants include:

• Cerebral palsy.
• Intrauterine infection.
• Pontocerebellar hypoplasia - need to look further for metabolic or degenerative disorders.
• Joubert's syndrome.
• Trisomies.
• Pyruvate dehydrogenase deficiency.
• Spastic ataxic syndrome.

Investigations
These should be guided according to the differential diagnosis based upon the initial assessment. This may include:

• Blood tests - FBC, LFTs, cholesterol, protein electrophoresis, copper and caeruloplasmin, immunoglobulins and glycoproteins.
• Electroencephalogram (EEG).
Electromyogram (EMG).
Imaging - MRI is the modality of choice.

Management and prognosis
This depends upon the underlying cause.

Further reading & references

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