CEREBELLAR ATAXIA:
A GUIDE FOR THE MEDICAL PROFESSION

Cerebellar ataxia can be thought of as a syndrome which has many different causes, the commonest in the UK being multiple sclerosis and alcoholic cerebellar disease. This guide is intended primarily for cerebellar ataxias which result from genetic causes, and degenerative ataxias which have no known cause. These are rare diseases. Most GPs never come across such a patient, and are understandably unfamiliar with the different aspects of these diseases. The purpose of this booklet is to provide GPs with information so they are in a better position to help cerebellar ataxia patients and their families with the many practical problems they face.

CLINICAL PRESENTATION

These diseases can manifest mainly in adult life, but also in adolescence or childhood. Certain features differ between patients and may help in making a precise diagnosis.

The following features are common presenting or early manifestations:
- Progressive ataxia of gait (usually broad based)
- Progressive limb ataxia including tremor
- Progressive slurring dysarthria
- Nystagmus

Later on during the course of these diseases:
- Ophthalmoplegia
- Dysphagia
- Parkinsonian features

A minority of patients may encounter:
- Decrease in visual acuity
- Cognitive decline

DIAGNOSIS AND INVESTIGATIONS

A careful history may make the diagnosis without further investigation, particularly if there is a clear mode of inheritance within the family. It may be relevant to exclude multiple sclerosis, posterior fossa tumours, alcoholic cerebellar ataxia or ataxia as a non-metastatic manifestation of malignancy. Ataxia may be caused by medication, particularly phenytoin. Vitamin E deficiency may cause a progressive ataxia and should always be excluded, even if there are no overt gastrointestinal problems.

Investigations may therefore include routine haematology and biochemistry, including liver function tests. Brain imaging is usually necessary. Screening for malignancy, vitamin B assay, other tests to exclude multiple sclerosis, and molecular genetic tests, may be used to confirm the diagnosis.

THE GENETIC ATAXIAS

These diseases are often classified on the basis of inheritance. Clinical diagnosis has now been aided by molecular genetic testing. This may pinpoint a specific genetic cause, which allows a precise diagnosis, or may exclude some types of ataxia, helping to refine the diagnostic possibilities.

For a full list of adult and paediatric inherited ataxias see Eur J Paed Neurol 2003: 7; 231-3.

AUTOSOMAL DOMINANT CEREBELLAR ATAXIAS

This group of genetic ataxias looks similar clinically, usually having a permutation of the clinical features outlined above. Onset can be from infancy to old age but most commonly is between the ages of 20-60. More than half of families have a mutation in a known gene. Most mutations have taken the form of a triplet repeat expansion (a stretch of DNA 2-3 times normal) existing in different genes. The responsible genes are numbered SCA1, SCA2, SCA3 etc, and over 25 subtypes are recognized, of which around 40% can be fairly easily tested for in the NHS. Testing for the remainder is complex; some known types may only be available as research, others may not yet have an identified gene, so testing may not be possible. Clinically, the gene SCA7 is important because visual failure may precede or accompany the ataxia, whereas vision is often preserved in the other ataxias.

Prognosis is variable but patients with later onset usually experience slower progression. As a guide, the ability to walk independently is lost approximately 15 years after onset.

AUTOSOMAL RECESSIVE ATAXIAS

The commonest autosomal recessive ataxia is Friedreich's ataxia (FA), which is described in another booklet.[1] However, there are other rare autosomal recessive ataxias. Clinically they can be distinguished from FA by the presence of reflexes, (usually lost in FA), and genetically by the absence of a mutation in the FA gene. Other recessive ataxias include ataxia telangiectasia, ataxia with ocular motor apraxia, ataxia with vitamin E deficiency and the recently identified ataxia with CoQ10 deficiency (which appears to respond to treatment with CoQ10 tablets).

EPISODIC ATAXIAS

These are also known as paroxysmal ataxias. They are characterised by episodes of ataxia including dysarthria, tremor and nystagmus lasting minutes to hours. The episodic ataxias are subdivided into two disorders on clinical and genetic grounds. In both disorders episodes are suppressed by acetazolamide. Patients need to be warned about the risk of nephrolithiasis on long term acetazolamide therapy; the incidence of this complication is estimated at 20%. Some patients may experience a progressive ataxia underlying the short lived episodes. Further details are beyond the scope of this text.

MITOCHONDRIAL DISORDERS

These involve mutations in the genes that are found in the mitochondria, the energy-producing compartments of cells. As each person inherits their mitochondria from their mother, this means that these disorders can only be passed down the maternal line. Most of the genes found in the mitochondria are involved in the production of energy, so generally mitochondrial disorders result from an incapacity to produce sufficient energy within cells, preventing them from doing normal functions. Some mitochondrial disorders have ataxia as a main symptom.

Examples of mitochondrial ataxia disorders are: NARP (neuropathy, ataxia, and retinitis pigmentosa),MELAS (mitochondrial encephalomyopathy, lactic acidosis with stroke-like episodes) and Myoclonus epilepsy with ragged red fibres (MERRF).

CEREBELLAR DEGENERATIONS OF UNKNOWN CAUSE

This syndrome has also been termed “idiopathic cerebellar ataxia” (ILOCA). Clinically this disease resembles the autosomal dominant cerebellar ataxias, but with no family history or detectable mutation. Extrapyramidal and autonomic features may be more prominent and may be improved by symptomatic treatment (although anti-parkinsonian drugs seldom help much). Course and prognosis varies markedly between patients.

Some patients initially diagnosed with this type of ataxia may then be given a specific diagnosis. For example they may be told they have multiple system atrophy (with cerebellar symptoms), or may be diagnosed as having gluten ataxia (which may respond to a gluten-free diet).

MANAGEMENT ISSUES

GENETICS

Expert assessment is required before ataxia is ascribed to genetic causes. Patients may require assessment by both a neurologist and a clinical geneticist. Inheritance has to be investigated both by pedigree analysis and by appropriate molecular genetic testing. Some patients with familial ataxia will not have an identifiable genetic defect and this may hinder genetic advice. By definition, patients with idiopathic late onset cerebellar ataxia have no affected relatives and will normally be given a low risk of passing on the disease to their children. However, even in the absence of family history someone can still be diagnosed as having an inherited cerebellar ataxia, so genetic tests should still be offered.

Relatives of patients with autosomal dominant cerebellar ataxia will have a risk of carrying the gene. This risk can be assessed by a clinical geneticist; in children of gene carriers this will be approximately 50%, depending on their age. In families with an identifiable mutation, both predictive and prenatal gene testing is technically straightforward, in a manner similar to Huntington's disease. The decision to undergo such testing is difficult and personal. Support in making such decisions is available from genetic counsellors. Testing may influence life assurance and job prospects. Knowledge of genetic status may be emotionally difficult as well as affecting relationships with others. At-risk relatives will normally be helped in coming

to their own decision by the genetic clinic. Testing for adult ataxias is not normally offered to those under 18 years of age, and should be postponed if there is significant depression or other stress factors such as divorce or, bereavement.

Asymptomatic or symptomatic gene carriers may consider prenatal testing during pregnancy, in order to abort an affected fetus. Ideally the gene carrier and his/her partner should be counselled in the genetic clinic prior to pregnancy to discuss technical aspects of prenatal testing and to come to a decision about proceeding with testing. If there is an identifiable mutation, testing may be achieved by chorionic villus sampling at the end of the first trimester, with the intention of a therapeutic termination of pregnancy should the fetus be carrying the gene. Whatever the result, this can be an emotionally traumatic experience and couples require sympathetic support.

Not all at-risk relatives seek genetic advice but those that do often find the genetic burden easier to bear once the situation has been fully and openly explained. Attending a genetic or neurology clinic carries no obligation to be tested, although most individuals find neurogenetic testing to be beneficial, whatever the result.

SPEECH AND SWALLOWING

Patients are often frustrated by dysarthria, which can lead those unfamiliar with them to conclude that they are under the influence of alcohol. Later in the disease dysarthria may cause communication difficulties. Expert speech therapy advice is important, and may lead to alternative communication strategies. Dysphagia becomes more common as the disease progresses. In advanced disease this can lead to weight loss or aspiration. The latter should be suspected if the patient swallows with difficulty, coughs after swallowing or has repeated chest infections. Patients often benefit from a swallowing assessment by a speech therapist and subsequent advice. In a minority of patients with advanced disease, palliation with percutaneous endoscopic gastrostomy (PEG) may be appropriate.

COLD FEET

Peripheral cyanosis, oedema and cold feet are common problems, reflecting a decline in muscle activity. Passive movements and attempts to keep the feet warm are often only partially successful.

SPHINCTER DISTURBANCE

This is uncommon except in late onset cerebellar degenerations of unknown cause.

DEPRESSION

All patients with progressive neurological disorders are susceptible to depressive illness. Low mood responds to antidepressants in the normal way. Counselling and non-drug treatments may also be helpful.

THERAPISTS

Modern management is aided by regular review with a multidisciplinary team, which may include neurologists, rehabilitation physicians and therapists. Close co-operation between professionals and the patient, family and carers is important. Physiotherapy is often valuable, particularly to preserve mobility. Advising on walking aids is difficult since the patient's major requirement is stability. Some patients may find a stick helpful. When walking is difficult, use of a "rollator" frame may be helpful. Referral to a wheelchair clinic for specialist seating advice is important at the appropriate stage of the disease. The key role of a speech therapist has been described.

Cerebellar ataxia patients benefit from regular assessments by an occupational therapist. Appropriate advice on home modifications and aids can help preserve independence as the disease advances.

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A patient leaflet 'Information on cerebellar ataxia' is available by post or from our website.

Ataxia UK
working with and for people affected by ataxia
Registered Charity Number: 1102391
(Formerly the Friedreich's Ataxia Group)

This leaflet was reviewed in November 2004 in collaboration with Professor Patrick Morrison, Consultant in Clinical Genetics, Belfast City Hospital Trust.

1 Friedreich's Ataxia: A Guide for the Medical Profession Ataxia UK, 2004