

## **FRIEDREICH'S ATAXIA: A GUIDE FOR THE MEDICAL PROFESSION**

Friedreich's ataxia (FA) is the most common of the hereditary ataxias in this country, but the prevalence in the UK is estimated to be only 1-2 in 50,000. Most GPs never come across an FA patient, and are understandably unfamiliar with the condition. The purpose of this booklet is to provide GPs with information so they are in a better position to help FA patients and their families with the many practical problems they face.

This guide was written in 1997 and updated in 2004. The discovery of the FA gene *frataxin* in 1996 has led to significant changes in the spectrum of disease recognised as being associated with FA. A genetic blood test along with genetic counselling is available to confirm diagnosis. Management of the condition has consequently improved.

Friedreich's ataxia is one of many hereditary ataxias. Much of the medical advice given here may not be applicable to ataxic patients who do not have FA.<sup>1</sup>

### **CLINICAL PRESENTATION**

Typically the disease manifests around puberty and usually between 2-16 years. In some early onset cases parents report that the child never walked normally although milestones are not delayed. Onset later than 25 years is unusual but access to molecular genetic diagnosis has shown that milder, late onset variants do exist, but are rare, and these rare mild variants may have an onset up to 50 years.

In most patients the presenting symptom is unsteadiness of gait. Alternatively the family may notice symptoms of generalised clumsiness or deterioration in athletic performance. Occasionally patients present with scoliosis and rarely with symptoms related to cardiomyopathy.

The following diagnostic criteria are those of Harding et al. (Brain 1989 104:589-620) with some modifications:

#### *Seen in all patients:*

- Progressive ataxia of limbs and gait
- Extensor plantar responses
- Nerve conduction studies showing motor velocities  $>40\text{ms}^{-1}$  in arms and absent sensory action potentials
- Dysarthria (often absent within 5 years of onset)

#### *Seen in more than two thirds of patients:*

- Areflexia
- Scoliosis
- Pyramidal weakness in lower limbs
- Distal loss of joint position and vibration sense in lower limbs
- Abnormal electrocardiogram

#### *Other features:*

- nystagmus, optic atrophy, deafness, distal weakness and wasting, pes cavus, diabetes.

## **DIAGNOSIS**

A diagnosis can be made clinically, usually by a neurologist, with the support of nerve conduction studies and ECG. Genetic analysis is readily available through most genetic centres and is used as a confirmation of the diagnosis in patients, and is essential in doubtful cases. Isolated vitamin E deficiency can produce an identical clinical picture without gastroenterological symptoms, and vitamin E assay is therefore important. Further investigations are usually unnecessary for diagnosis, although may be necessary for full assessment.

## **MANAGEMENT ISSUES**

### *GENETICS*

Friedreich's ataxia is an autosomal recessive condition. Normally patients will be at low risk of passing on the condition to their children, unless their partner is related. There appear to be no specific complications of pregnancy; about one fifth of patients reproduce.

Siblings will be at risk of the disease and prenatal diagnosis is available if the patient's parents are considering having further children. Usually, however, families are complete by the time a child is diagnosed as having FA.

Over 95% of patients have an expansion of DNA within each of the two FA genes (a much larger stretch of DNA than usual). This is very easy to identify within a couple of weeks of the genetic test. More rarely some patients may have a point mutation in one gene (a very small change in the FA gene which may be found only using specialist gene sequencing techniques available at just 1 or 2 genetic centres in the world, and may therefore take much longer to analyse). The size of the expansion of the FA gene may give some indication of severity as very large expansions confer earlier onset, and very small expansions confer a later and mild onset. The gene size in most patients is similar. The gene is usually only measured in cases where it is either very large or very small, to help with diagnosis and management.

### *PROGNOSIS*

The rate of progression is variable, but typically patients become chairbound 15 years after onset of symptoms. Age at death is even more unpredictable, depending on the presence of complications and other factors. Whereas patients do die prematurely of the disease, there are increasing numbers living beyond the fifth decade.

### *CARDIOMYOPATHY*

This is present in the majority of FA patients. The typical ECG pattern includes T wave inversion in the inferior and lateral chest leads. Echocardiography typically shows a symmetric concentric ventricular hypertrophy. Exertional dyspnoea may be explained by respiratory factors and neurological disability as well as cardiac causes.

Otherwise, cardiac symptoms are relatively rare and occur late in the disease. Cardiac failure and arrhythmias usually require cardiological advice.

### *ORTHOPAEDICS*

Scoliosis is common and may be severe, especially in early onset cases. Referral to an orthopaedic surgeon with an interest in scoliosis is advised. Surgery may be helpful in carefully selected cases, particularly when the scoliosis is progressive. Perioperative bedrest should be minimised. About 50% of patients have pes cavus or equinovarus deformity of the feet. Surgical procedures may be helpful if the deformity causes symptoms.

### *DIABETES*

Diabetes occurs in approximately 10% of patients. Most but not all such patients require insulin therapy.

### *COLD FEET*

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

### *SPHINCTER DISTURBANCE*

Constipation is common and is often related to immobility. Urinary urgency is seldom severe.

### *DEPRESSION*

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

### *THERAPISTS*

Modern management is aided by regular review with a multi-disciplinary team, which may include neurologists, community and hospital paediatricians, rehabilitation physicians, genetic advisors and other therapists. Close co-operation between professionals and the patient, family and carers is important.

Physiotherapy is often valuable, particularly to preserve mobility. 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. Patients benefit from a thorough assessment from an occupational therapist, especially when the disease becomes disabling. Liaison with school authorities, often with the help of a community paediatrician is important in school age children. Referral to a social worker and speech and language therapy is often helpful.

For more information contact:

Ataxia UK  
Winchester House  
Kennington Park, Cranmer Road  
London SW9 6EJ  
Tel: +44 (0)20 7582 1444 FAX: +44 (0)20 7582 9444 EMAIL  
enquiries@ataxia.org.uk  
[www.ataxia.org.uk](http://www.ataxia.org.uk)

A patient leaflet 'Information on Friedreich's 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.