FRIEDREICH ATAXIA

DEFINITION AND PREVALENCE

Friedreich ataxia (FA) is an inherited disorder affecting the spinocerebellar tracts, dorsal columns, pyramidal tracts, and, to a lesser extent, the cerebellum and medulla. The progressive dammages are reflected in a series of problems with the nervous system, speech and walking. FA may induce heart disease and diabetes.

FA is the most common hereditary ataxia. It occurs with a prevalence of approximately 1 in 50 000 in Caucasian populations, but is very rare among sub-Saharan Africans and virtually does not exist in the Far East. FA affects both men and women equally. 1 in 110 is a carrier of the pathological gene.

ETIOLOGY

FA is inherited as an autosomal recessive disorder. FA is caused by mutations in the FRDA gene which encodes the protein frataxin. Frataxin is necessary for the proper functioning of mitochondria. The pathogenic mutation is an expanded GAA triplet repeat in intron one of the FRDA gene in 98% of mutant alleles. The fact that one mutation accounts for the vast majority of FA means that there is a relatively simple diagnostic test available for this disease.

The caused mitochondrial dysfunction leads to degeneration of nerve tissue in the spinal cord, in particular sensory neurons essential for directing muscle movement of the arms and legs. The spinal cord becomes thinner and nerve cells lose their myelin sheath.

DIAGNOSIS

Diagnosis is made through a thorough physical examination that may include tests for reflex and sensory responses. Laboratory tests such as the electromyogram and nerve and muscle biopsies may also be used to confirm the diagnosis. In addition, the physician may take an electrocardiogram to determine if abnormalities in the heartbeat exist, and blood and urine analyses may be made to check for diabetes.

CLINICAL PICTURE

In general the first symptoms are manifested before adolescence and include incoordination of limb movements, dysarthria, nystagmus, diminished or absent tendon reflexes, Babinski sign, impairment of position and vibratory senses, scoliosis, pes cavus, and hammer toe. The typical clinical triad of hypoactive knee and ankle jerks, signs of progressive cerebellar dysfunction, and preadolescent onset is in most cases sufficient for the diagnosis.

There are conditions associated with FA that do not result from the degeneration of nerves. Heart disease is sometimes in very severe forms. Abnormalities in heartbeat rhythm and diminished strength of the heart muscle have been noted in a large percentage of FA patients, with palpitations and dyspnea (shortness of breath) the most common found symptoms. Diabetes mellitus, characterised by abnormally high blood and urinary sugar levels, is another condition that may attend FA.

Symptoms typically begin sometime between the ages of 5 to 15 years. Their progression is slow. Lower limbs are more affected. FA usually results, within eight to ten years following the onset of symptoms, in an inability to walk. Occasionally, the disease goes into spontaneous remission, which sometimes lasts five to ten years or longer. Remissions, however, are uncommon.

TREATMENT

At present there is no generally accepted treatment for FA, all therapies are symptomatic and response to particular clinical sign.

The mitochondrial dysfunction in AF has some treatment perspectives with *idebenone*, a free-radical scavenger. This rationale is based on the fact that the frataxin gene is involved in the regulation of mitochondrial iron content. The in-vitro data have suggested that both iron chelators and antioxidant drugs, that may reduce iron, are potentially harmful in FA patients. Conversely, preliminary findings suggest that *idebenone* protects heart muscle from iron-induced injury. Clinical data are still partial as the drug is approved for use in Canada, but is still under investigation in the EU and USA.

A 4-year follow-up on 10 FA patients treated with *coenzyme Q10* and *vitamin E* showes a substantial improvement in cardiac and skeletal muscle bioenergetics and heart function. Antioxidant treatment resulted in sustained improvement in mitochondrial energy synthesis that was associated with a slowing of the progression of certain clinical features and a significant improvement in cardiac function. More recent studies direct the attention towards *L-carnitine* as a promising substance for treatment of FA patients.

Orthopedic intervention, which may include surgery, can alleviate scoliosis, and orthopedic appliances and physical therapy help prolong ambulation.

REHABILITATION AND FOLLOW-UP CARE

Physical therapy has a proven positive impact on managing the symptoms of AF. A team of neurologist and specialists in physical rehabilitation and occupational therapy prepare an individual programme tailored to the patiet's abilities and health status.

A special target of physiotherapy is maintaining the capacity to walk alone. Low-intensity strengthening exercises are included to preserve the functionality of upper and lower extremities and to prevent immobility. Fatigability should be carefully monitored. Stabilising back and waist exercises help to control posture and reduce spinal curvature. Balance and coordination training may be conducted using visual feedback. Exercise can imitate everyday activities such as moving, personal hygiene, cooking, etc. In addition, the patient should be trainined to avoid the risk of falling. A speech therapist could be also included to manage linguistic and oropharyngeal problems.

Mobility aid devices can be also considered, as they may lead to a higher degree of autonomy in some cases.

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