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My46 Trait Profile

Friedreich ataxia

Friedreich ataxia is a rare genetic condition characterized by damage to the nerve cells causing a progressive loss of balance and coordination of movement. It is caused by mutations in the FXN gene which makes a protein called frataxin.

Characteristics of Friedreich ataxia

Friedreich ataxia (FA) is a rare progressive disease affecting the brain and nervous system resulting in movement problems. FA affects about 1 in 50,000 individuals. It is estimated that there are 5,000 to 6,000 individuals with FA in the U.S. and 10,000 to 15,000 worldwide. FA was originally characterized as a neurodegenerative disease because of the primary feature – ataxia or loss of balance and coordination in the lower and upper limbs which leads to loss of independence with many activities of daily living. However, FA is a multi-system condition that can affect many organs including the heart, pancreas and other organs.

Most often the first symptoms or features of FA that bring an individual to a doctor are loss of balance or difficulty with walking or running. Other neurologic symptoms can include a loss of sensation in the hands and feet, loss or absence of reflexes, slurring of speech, and extra eye movements or what looks like fluttering of the eyes. Optic atrophy, a type of vision loss that occurs rapidly, is quite severe and leads to blindness, is seen in about 5% of individuals with FA. The loss of neurologic function is progressive with most individuals losing the ability to walk independently about 6-8 years after diagnosis. While FA is a neurologic condition, intelligence and psychological health are not primarily affected.

There are other organ systems affected in FA. Heart problems are common in FA. Nearly all individuals with FA have a difference on their EKG called an inverted T-wave; this difference is often not clinically significant but a sign of the condition. About 50% of individuals will develop a more serious condition such as a thickening of the left ventricle called hypertrophic cardiomyopathy and/or abnormal heart rhythms or arrhythmias. These heart conditions can also be progressive and lead to early death.

Scoliosis (curvature of the spine) is common in FA and in about 50% of individuals requires surgery for correction. Another common musculoskeletal feature is high arch feet (pes cavus). Individuals with FA are at increased risk for diabetes and insulin resistance. Hearing loss, specifically a sensorineural type of hearing loss that causes impaired temporal processing, is significant in later stages of the disease and is recognized by the individual as having hearing difficulty in public settings where there is background noise.

Nearly all individuals with FA experience significant fatigue. This fatigue results in individuals requiring more hours of sleep per night or needing naps more frequently and the fatigue impacts quality of life.

The onset and severity of symptoms varies among individuals. Childhood onset FA is associated with more rapid progression with symptoms appearing between the ages of 5-15 years. Late onset FA is defined by onset of symptoms after age 20. Late onset is associated with slower progression of neurological symptoms and mild phenotype including lower risk for scoliosis and cardiac abnormalities.

Diagnosis/Testing

Changes or mutations in a gene called FXN cause FA. This gene makes a protein called frataxin. The FXN gene contains a three-letter code, GAA, that is repeated over and again, and thus it is known as a “GAA repeat.” The number of

GAA repeats can be different from one person to another. Individuals who do not have FA usually have between 5 GAA repeats (e.g., GAA-GAA-GAA-GAA-GAA) and 33 GAA repeats. However, individuals with FA usually have an abnormally high number of GAA repeats that can range from over 66 to 2000 repeats. A large number of GAA repeats is known as an expanded GAA repeat. More than 95% of individuals with FA have an expanded GAA repeat in both copies of the FXN gene. Approximately 5% of individuals have an expanded GAA repeat in one copy of the FXN gene, and another type of mutation in the other copy of the FXN gene. The larger the expansion, the earlier and more severe the symptoms are in affected individuals. Genetic testing is the gold standard for diagnosis.

Management/Surveillance

Comprehensive clinical management guidelines for FA are currently under development and anticipated to be available in the fall of 2013.

Current management recommendations include yearly heart ultrasounds (echocardiograms), tests that checks for problems with electrical activity of the heart (EKGs), blood tests to measure glucose, scoliosis screening (especially in children ages 7-18), hearing and vision screening, as well as physical, occupational and speech therapy. Most children diagnosed with FA require mobility aids such as a cane, walker, or wheelchair by their teens or early 20s.

Many individuals with FA take vitamins and antioxidants such as co-enzyme Q10, vitamin E, and Idebenone. No clinical benefit has been proven in placebo controlled trials, however individuals report feeling more energy and improved quality of life when adding these supplements.

Due to the heart condition associated with FA certain surgical procedures and general anesthesia can be of greater risk. Individuals with FA are also known to have exacerbation or worsening of symptoms during a viral illness.

While there is no treatment for FA, there are potential new treatments that are early testing or clinical trials. It is important for individuals who are diagnosed with FA learn about the research progress and discuss with a knowledgeable health care provider about the risks and benefits of participating in this type of research. To learn more about clinical trials in FA there are several sources (e.g., ClinicalTrials.gov, http:// www.curefa.org/registry).

Mode of inheritance

FA is inherited in an autosomal recessive pattern. This means that an individual has to inherit two FXN mutations (i.e., one from each parent) to be affected with FA. A carrier is an individual who has one FXN mutation and one normal copy of the gene. Carriers have no symptoms of FA. If both parents are carriers of a FXN mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with FA.

Risk to family members

Parents of a child with FA are carriers of FA. If a sibling of a child with FA is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of FA.

Genetic counseling and carrier testing is recommended for at risk relatives of child-bearing age.

Special considerations

None

Resources

Friedreich's Ataxia Research Alliance – FARA
http://www.curefa.org
Muscular Dystrophy Association
http://www.mdausa.org
National Ataxia Foundation
http://www.ataxia.org

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