Friedreich's Ataxia and rehabilitation: A Review of Literature

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Abstract:

The most prevalent inherited ataxia is Friedreich's ataxia. The development of a GAA triplet inside the first intron of the frataxin gene on chromosome 9q13 is to blame. Homozygosity for a GAA repeat expansion can be detected in intron 1 of the FXN gene in around 96 percent of affected persons. Reduced iron-sulfur cluster formation and mitochondrial ATP generation, as well as increased mitochondrial iron and oxidative stress, are all caused by a lack of frataxin protein. Inflammation has recently been established as a crucial element in Friedreich ataxia development. Pharmaceuticals that boost frataxin levels, protein and gene replacement therapies, antioxidants, iron chelators, and inflammatory modulators are some of the treatments available. Dysarthria, muscle weakness, impaired proprioception and vibration, peripheral neuropathy, absent lower limb response, ataxic gait, and other symptoms of Friedreich's ataxia can be treated with physiotherapy.

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Introduction:

Friedreich ataxia (FA) is the most frequent kind of hereditary ataxia, accounting for almost half of all cases. (1,2) The condition usually starts in childhood, with an average start age of eight years and a ten-year duration. (3) FRDA is a degenerative autosomal recessive condition. (4)

In FRDA, large sensory neurons in the dorsal root ganglia degenerate early, followed by sensory posterior columns degeneration, spinal-cerebellar tracts degeneration, and cortical-spinal motor tracts degeneration, as well as atrophy of large sensory fibers in peripheral nerves. (5)

The genetic etiology of FRDA was found in 1996 as homozygous/compound heterozygous mutations in FXN (previously known as X25 and FRDA). (6) While most people have less than 36 GAA repeats, those who have been impacted have range from 56 to 1300. (7, 8)

The number of GAA repeats in the smaller allele (GAA1) is negatively associated to the age of symptom beginning and a number of outcomes, including cardiomyopathy, diabetes mellitus, scoliosis, and the period from symptom onset to the need for a wheelchair for mobility. (7, 9)

The frataxin (FXN) gene on chromosome 9 has an aberrant quantity of trinucleotide repeats in patients with FA. (10) Frataxin is a protein that aids in the creation of mitochondrial adenosine triphosphate (ATP) synthesis and iron store management enzymes. Gene repression and a decrease in frataxin concentrations are caused by the troublesome trinucleotide repeats in FA. Highly active cells that rely on ATP generation include neurons, cardiomyocytes, and pancreatic beta cells. (11)

Electrocardiographic or echocardiographic evidence of hypertrophic cardiomyopathy can be found in a substantial percentage of FRDA patients, and cardiac involvement is the most common cause of early mortality. (12)

In the left ventricle, myocyte hypertrophy, extensive fibrosis, and localised myocardial necrosis are all pathological abnormalities. It usually begins with awkwardness in walking. (f4) (1) autosomal-recessive inheritance, (2)

Extensor plantar response onset before the age of 25, (3) progressive limb and gait ataxia, (4) electrophysiologic evidence of axonal sensory

Neuropathy, lacking tendon reflexes in the lower extremities, followed by (5) dysarthria (within 5 years of onset), and (6) areflexia in each of the four limbs are all important clinical features. (8) pyramidal weakening of the legs, (7) distal loss of position and vibration sensitivity (9) Loss of ambulation occurs 7.4–15.5 years after the disease first appears. Scoliosis and pes cavus affect about two-thirds of the patients, while diabetes and glucose intolerance affect one-third. Hearing loss or optic atrophy are detected in around 10% of people. Cardiomyopathy is the most common cause of mortality. The "typical" or "classic" form of the disease is defined as patients who exhibit all of Harding's clinical signs. (13–17)

Clinical diagnosis

Before the age of 25, the essential age of onset Ataxia of the gait and limbs develops over time. Knee and ankle jerks aren't present. Neurophysiology axonal image Dysarthria is a type of dysarthria that affects (if after five years from onset)

in addition (present in over 66 percent) Scoliosis Lower-limb pyramidal weakness Arms with no reflexes On inspection, there is a large sensory loss in the fibres, as well as an abnormal ECG.

Others (less than a half of a percent) Nystagmus Atrophy of the optic nerve Deafness Amyotrophy at the distal end Diabetes pes cavus Harding's criteria (table 1) were universally accepted and remain valid today, but we can now reinterpret "atypical" situations in light of readily available genetic data. Friedreich's ataxia is marked by cardiomyopathy, which is the most conspicuous non-neurological feature. The exact number of people who have cardiomyopathy is unknown. However, a study that looked at hearts in detail found that over 90% of them had abnormalities, although even the clinical significance of some of the slight differences is undetermined. In roughly 65 percent of patients, an abnormal electrocardiogram (ECG) is seen, with widespread T wave inversion in the inferolateral chest leads. The most prevalent echocardiographic abnormality is concentric ventricular hypertrophy. Regardless of the fact that cardiac arrest is a late onset condition, a specialist referral may be required because arrhythmias are a major cause of mortality and morbidity. As a result, an ECG should be performed on the patient. Diabetes affects around 10% of the population, hence a blood sugar calculation should be included.

Nerve conduction studies are used to diagnose sensory neuronopathy without sensory motion potentials. This distinguishes Friedreich's ataxia from the Roussy-Levy variation of hereditary motor sensory neuropathy type 1, which causes sensory ataxia with missing tendon reflexes and was once thought to be a "forme-fruste" of Friedreich's. In the early 1980s, vitamin E deficiency was linked to a variety of illnesses, including abetalipoproteinemia, chronic liver disease, and cystic fibrosis. Patients with vitamin E deficiency may develop a spinocerebellar syndrome that resembles Friedreich's ataxia but differs from it due to other characteristics. A clinical sign to the presence of Friedreich's ataxia is a distinctive titubation, which is rarely seen in typical Friedreich's ataxia. Although the rarity of this illness, vitamin E supplementation can result in a little improvement or, at the at least, a halt in the evolution of the clinical syndrome, thus it's always worth testing vitamin E levels in such patients. Because absorbance is normal, a direct issue about vitamin supplementation should be posed. A normal vitamin E level can be misleading if vitamin E supplements are consumed. If the spinocerebellar syndrome is compounded by other neurological problems, such as dementia, other disorders such as hexoseaminidase A deficiency, abetalipoproteinaemia, adrenoleucodystrophy, and similar ailments should be explored.

However, the condition has a relentless progression, with dysarthria and pyramidal weakness emerging just a few years after onset, preceded by jerky eye movements that eventually lead to nystagmus. Between 10 to 15 years of starting, the patient is typically confined to a wheelchair. It's important to note that patients may only be diagnosed with cardiomyopathy after seeing a cardiologist. There were two recent cases in which the choreiform movement disorder was present but there were no signs of ataxia. Friedreich's ataxia was the underlying condition, as evidenced by the loss of reflexes in both, as well as scoliosis in one and cardiomyopathy in the other.

GENETIC DIAGNOSIS

Clinical diagnosis is still important, and it was discovered that all individuals identified with the strict criteria were homozygous for the expansion. Thanks to the availability of a relatively simple direct genetic test, the diagnosis can now be explored in more unusual situations. Genetic testing has been shown to be helpful in detecting the correct diagnosis and directing appropriate screening tests, such as a cardiac examination and a blood sugar assessment. Perhaps the most exciting development since the gene's identification is the rapid improvement in the understanding of the protein. There is reason to be positive about finding a treatment that works if it turns out to be a mitochondrial protein involved in iron transport, which appears to be the case.

Genotype-phenotype correlations

The introduction of a diagnostic test has allowed the clinical phenotype to be re-evaluated. It was recently discovered that a small number of Friedreich's ataxia patients had residual tendon reflexes. Although the majority of patients present before the age of 25, it can happen at any age, with the oldest patient being 51 years old. According to research involving large numbers of patients, the duration of repetition size is a factor of the age of onset and so affects the severity of the disease to some extent, with cases with early onsets likely to progress more quickly. However, this link only applies to groups of patients and is ineffective for counselling a single patient or family. Cardiomyopathy appears to be linked to the length of the loop, but more research is needed to identify the exact correlation. Subsequently discovered three families in which inheritance appeared to be dominant at first because one of the parents in each case had ataxic syndrome. In one of these families, the presence of two aberrant alleles in the paternal generation and two in the affected offspring demonstrated pseudodominance, indicating that a patient married a carrier. Friedreich's ataxia is present in the offspring of the other two families, both clinically and genetically. The fathers, on either hand, suffer from a more complex ataxia that manifests later in life. Because they are both heterozygotes for the expansion, it's likely that they both have point mutations that are causing their phenotypic differences, or that they have ataxia for another rationale.

THERAPEUTIC INTERVENTION:

Patients with FRDA can improve their aerobic fitness by riding stationary for 20 to 25 minutes at 70% to 85% of their maximum heart rate, as determined by a graded exercise test. Based on their individual limitations, physical therapists can assist people with FRDA in selecting the most appropriate community exercise and leisure activities. (18) When you're on the mend, it's vital to maintain your biomechanical alignment. Orthotics or surgery are routinely used to treat orthopaedic diseases such as foot deformities and scoliosis, which can provide a temporary improvement in function. The treatment plan should include daily range of motion checks, as well as muscle length and soft-tissue extensibility. A home fitness programme and family education for follow-through would almost certainly be included in this treatment approach. Physical therapists are frequently involved in selecting assistive or adapted equipment for use during functional tasks. When a walker is recommended for maintaining gait independence, utilising one with a reverse-brake system has been demonstrated to lower the number of falls. (19) When a wheelchair is indicated as a primary means of transportation, therapists may propose that patients and families first choose a power scooter for community transit and a manual wheelchair for inaccessible areas encountered in regular life. (20Task-oriented reaching exercises for bimanual upper-extremity training were among the UE activities. This type of intervention was chosen since it is generally known that bimanual, synchronous movements are intrinsically stable and preferred coordination patterns. 34,35 These exercises progressed from 2 sets of 8 repetitions to 4 sets of 12 repetitions and included rhythmic reaching for a ball (shoulder flexion from 80° to 170°) and object placement on a table (horizontal shoulder adduction 0° to 45° and abduction from 0° to 45° while at 80° of shoulder flexion). (21)

LE stretching of the hip extensor and ankle plantar flexor muscle groups (2 to 3 sets for 60 seconds) can help maintain appropriate LE alignment in a wheelchair, improve posture while sitting for long periods of time, and increase ankle dorsiflexion during the stance phase of

locomotion. Functional strengthening can be used to correct the modest weakness identified by the MMT and to aid upright mobility. Bridges with a therapy ball for LE stabilisation, wall squats with a therapy ball against a wall, and single limb hip flexion while supine) and trunk muscle groups (seated hip flexion and extension with a neutral lumbar spine) therapeutic exercises can be performed, progressing from two sets of eight repetitions to three sets of eight repetitions. Gait training was done with a Rollator wheeled walker from month one to month nine (RWW; with a standard braking system; Sunrise Medical Inc., Longmont, CO). Good weight shifting, consistent step length, maintaining the line of progression, increasing step length, managing gait speed, and maintaining proper trunk and pelvic alignment when walking are all emphasised in this intervention (2 to 3 bouts of ambulation for 100 ft). You can enhance your gait with the UStep Walking Stabilizer (USWS; a walker with a reverse-braking system and tension-controlled wheels; In-Step Mobility Products Corp., Skokie, IL). Until the hand controls are depressed, the USWS reverse-braking mechanism maintains the brakes engaged. The tension-controlled wheels also allow the user to alter the amount of resistance required to roll the walker, resulting in a more consistent and controlled gait speed. Muscle groups in the hips and trunk are strengthened (isodynamic exercise using elastic bands and mat activities) (22)

Friedreich's ataxia patients can benefit from orthotic shoes to help them walk better. Walking distance increases, falls decrease, stability improves, and speed, step length, and cadence improve. (23)

Conclusion:

Progressive ataxia, missing lower limb reflexes,

Upgoing plantar responses, peripheral sensory neuropathy and loss in trunk control are all common clinical characteristics. Physical therapists' major goal is to improve individual participation as much as possible, regardless of environmental circumstances, while taking into account the disease's progressive character. Following recovery, the amount of time spent ambulating in the community increases.

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