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A case report on friedreich ataxia in a tertiary care teaching hospital

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Abstract
Friedreich ataxia (FA) is a progressive neurodegenerative disorder and is characterized by an autosomal recessive trait inducing spinocerebellar ataxia. It is the most common autosomal recessive ataxia affecting one individual in 50,000 with an estimated carrier prevalence of about 1:110. Initial symptoms usually seen in children and teenagers include loss of balance, coordination and fatigue. As the disease progresses patient develop dysarthria, vision and hearing loss, cardiomyopathy and diabetes. Scoliosis is often seen early in the disease and a significant proportion of patients need surgical correction. The two major complications of FA are cardiomyopathy and diabetes mellitus. In the present case A female patient of age 19 years with chief complaints of weakness in both lower limbs, difficulty in walking since 3 ½ years and mild swelling while walking since 3 years, difficulty in climbing stairs. The patient is unable to stand and walk without support. The patient had scoliosis to the right side. Unlike usual presentation of friedreich ataxia, this patient had no difficulty in hearing, no visual abnormalities. Patient was advised with rehabilitation and capsule Rejunex.

Keywords: friedreich ataxia (FA), teaching hospital, tertiary care

Introduction

FA was described in five papers by Nicholaus Friedreich over the period of 1863-1877 as FA is a debilitating, life-shortening, degenerative neuromuscular disorder [1]. FA is a progressive neurodegenerative disorder affecting both children and adults [2]. FA is usually manifested before adolescence [3]. The mean age of onset in classical FA is between 10 and 16 years, late onset and very late onset FA develop after the ages of 25 and 40 years respectively [4]. There is no sex predilection and it can affect both males and females [5]. It is caused by severely reduced levels of frataxin followed by mutations in frataxin gene as a result of large GAA triplet repeat expansion within the first intron of the frataxin gene [6].

The hall mark clinical features of FA include progressive afferent and cerebellar ataxia, dysarthria, impaired vibration sense, proprioception, absent tendon reflexes in lower limbs, pyramidal weakness, scoliosis, foot deformity, cardiomyopathy and diabetes mellitus [7]. 98% of the patients have an expansion of GAA trinucleotide repeat located within the first intron of the FXN gene; the other 2% are due to point mutations in the FXN gene. Normal individuals have 5 to 10 GAA repeat expansions whereas affected individuals have 70 to more than 1000 GAA triplets [3]. FA is the result of accumulation of iron in mitochondria leading to excess production of free radicals, which results in cellular damage and death.

The two major complications of FA are cardiomyopathy and diabetes mellitus [1]. A significant proportion of patients (two-thirds) develop cardiomyopathy. About 10% of them develop diabetes mellitus, while 20% have glucose intolerance. The mean life span of FA patients is approximately 35 years. No effective treatment for FA is available so far [3]. A phase II clinical trial is currently ongoing, which will give an indication of whether a simple vitamin supplement could be an effective, safe and reliable treatment for this debilitating disorder [8].

Case Report

A female patient of age 19 years with chief complaints of weakness in both lower limbs, difficulty in walking since 3 ½ years and mild swelling while walking since 3 years, difficulty in climbing stairs. The patient is unable to stand and walk without support. The patient had scoliosis to the right side. Unlike usual presentation of friedreich ataxia, this patient had no difficulty in hearing, no visual abnormalities. Examination showed that the vitals are stable. Diagnosis of friedreich ataxia was done on the basis of patient history and examination as genetic conformation facilities were not available. Cranial nerves and fundus were normal. ECG [electro cardiogram] showed the T-wave abnormality with possible anterolateral ischemia. Thyroid function test, blood sugar profile, liver function tests, urine examination and complete blood profile were within normal limits. Patient was rehabilitated with physiotherapy to provide flexibility, strength and range of movement of muscles and aerobic exercises were practiced to avoid fatigue. The patient is on Cap. Rejunex (OD).

Discussion

Friedreich ataxia is a highly disabling disease. Neurological features characteristically include progressive gait and limb ataxia, dysarthria, weakness, ocular fixation instability and deep sensory loss. Non- neurological involvement includes hypertrophic cardiomyopathy, diabetes mellitus and skeletal

deformations such as kyphoscoliosis, pes cavus and pes equinovarus [9].

FA is a slowly progressive disorder. Usually the onset of symptoms is during adolescence with unsteadiness of gait. Disease onset before the age of 20 and cardiac involvement are associated with faster progression of neurological symptoms. Interestingly, clinical symptoms do not progress at the same rate. Dysarthria manifests within 10 to 15 years and diabetes within 16 years where as loss of proprioception takes more than 40 years to develop [10].

Musculoskeletal complications are common in FRDA and scoliosis affects most patients. Bracing has not been shown to affect prognosis, it may help delay surgical correction in young children [4]. Scoliosis has a prevalence of 63% to 100% in patients with FA. Males and females are equally affected. Scoliosis develops within a few years of onset of ataxia [5].

Heart malfunction is the primary cause of early mortality in FA: mean life expectancy is reduced to approximately 40 years and 60% of the patients with FA will suffer from cardiac complications [11]. Bertoni *et al*., showed 45% of cardiac involvement in FA patients presented as left ventricular hypertrophy. Concentric left ventricle thickening was detected in 68% of children with FA by Alborias *et al*. Gunal *et al*., also reported high percentage (58%) of cardiomyopathy in children with FA [3]. The most common cause of death in FRDA is cardiac dysfunction, namely congestive heart failure or arrhythmia and average age at death was reported as 36.5 years in a large retrospective study [4]. So every FA patient should be regularly followed for cardiac diseases. Echocardiography is recommended at every visit and the patient is managed accordingly.

FA is associated with high incidence of diabetes mellitus. 23% of FA patients were found to have diabetes and 4 developed diabetic ketosis terminally. Clinically apparent diabetes is seen in approximately 18% of affected individuals, while impaired glucose tolerance is present in upto 39% of FA patients (3). Younger age at onset and longer disease duration increase the risk of DM [4]. The prevalence for diabetes among FA patients varies between 8 to 49%. Manifestation of diabetes is usually a late event in the course of FA (mean 15 years after onset) [10]. So the patients with FA should be regularly reassessed for DM and counselled regarding life style modifications.

Ptosis is present in about 10% of patients. Vision is impaired in one fifth of patients. FA may even lead to blindness in late stages. Hearing problems are common and may worsen over time. Foot deformities may significantly interfere with mobility in 55 to 90% patients [10]. There were no such complications in our patient.

Over 20 potential therapeutics have been tested in clinical trials in FA patients, but no drug has been approved for this disease [11]. No effective treatment for FA is available so far. Gene therapy and protein replacement strategies for FA are promising approaches for the future [3]. Restoring reduced frataxin levels is an appropriate approach for slowing down or stopping FA [10].

Physiotherapy provides an important means of maintaining balance, flexibility, strength and accuracy of limb movements. Aerobic exercises may help to improve weakness and fatigue. Rehabilitation may help counteract the effects of ataxia, weakness and spasticity in FRDA patients [4].

Conclusion

There is a need to identify the drugs that are likely to be effective for the treatment of FA. Early identification of the patients who are at risk of developing FA with related complications and providing proper therapeutic intervention by physiotherapy, aerobic exercises and rehabilitation at an earlier stage of the disease can reduce the disease progression.

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