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Case Report *Medical research*

A Case Report on Friedreich's Ataxia

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ABSTRACT

Friedreich's ataxia is a genetic disorder that causes certain nerve cells to weaken over time. Gene mutation at 9q13 and 9p23-p11. GAA trinucleotide repeats expansion of intron 1 from 70 to more than 1000 GAA triplets, and uncontrollable decreased vitamin E levels. Friedreich's ataxia also affects the heart, bones and pancreas cells that produce insulin. Loss of coordination, fatigue, vision impairment, aggressive scoliosis, DM and serious heart condition (cardiomyopathy) are the major signs and symptoms. This is a case review presenting: A 25-year-old male patient admitted in a general medicine with the chief complaints of breathlessness and pedal edema since 10 days and he was previously treated for upper respiratory tract infection. The patient was swaying to the right associated with curvature of the spine. These symptoms progressed slowly and then noticed to have difficulty in lifting both upper and lower limbs simultaneously in both proximal and distal regions. Difficulty in turning in bed, deterioration of vision since last three years, presently only able to appreciate light. He was found to have high sugar level since last year. Past medical history reveals that known case of DM and dilated cardiomyopathy since one year. Based on the patient medical history, physical examination, neurologic examination, neuroimaging, three-generation family history, and molecular genetic testing the patient complaints were diagnosed as friedreich's ataxia. Patient initially managed with symptomatically followed by physical therapy. Antioxidant such as vitamin E, coenzyme q10 and idebenone were given to delay the disease progression. Medications to lower the blood sugar, heart disease (ACE inhibitor) prescribed to reduce the co-morbidities with Friedrich's ataxia. Surgery is preferred to correct bony deformities. The patient improved after 17 days of therapy. Patient discharged on request and advised to go for eye check-up. Regular physiotherapy and speech therapy recommended improving their cognitive functions.

Keywords: Friedreich's ataxia, Gene mutation, Scoliosis, Cardiomyopathy, Pleural effusion.

INTRODUCTION

Friedreich's ataxia is an autosomal recessive inheritance (ARI) disorder that arises when the FXN gene encloses amplified intronic GAA repeats (an example of Trinucleotide repeat expansion). The FXN gene encodes with the protein called frataxin. Frataxin is an iron-binding protein responsible for forming an iron–sulfur cluster. One result of frataxin deficiency is mitochondrial iron burden which can cause destruction of many proteins. GAA repeat expansion causes reduced levels of frataxin. [1] Low frataxin levels lead to inadequate biosynthesis of iron-sulfur clusters that

are essential for mitochondrial electron transportation and assembly of functional aconitase and iron dysmetabolism of the entire cell. In normal individual frataxin is encoded by FXN gene, a mitochondrial matrix protein. This globular protein consists of two α helices and seven β strands and is highly conserved, occurring in all eukaryotes and some prokaryotes. [2] Frataxin has a variety of known functions. In electron transport chain, frataxin assists iron-sulfur protein synthesis, which is ultimately generated adenosine triphosphate (ATP), the energy currency necessary to carry out metabolic functions in cells. Frataxin also regulates iron transfer in the mitochondria in order provide a proper amount of reactive oxygen species (ROS) to maintain normal processes. [3] Without frataxin, mitochondria fail to produce the energy, and more ROS to be created due to excess iron, leading to further cell damage. Symptoms typically begin between the ages of 5 and 15 years, although they sometimes appear in adulthood and on rare occasions as late as age 75. The gait ataxia is a first symptom usually appears, or difficulty in walking. The ataxia gradually worsens and slowly spreads to the arms and the trunk. There is so often loss of sensation in the extremities, which may spread to other parts of the body. Other features include loss of tendon reflexes, especially in the knees and ankles, poor coordination, such as gait disturbance; it can also lead to scoliosis, heart disease and diabetes, but does not affect cognitive function. [4] Slowness and slurring of speech (Dysarthria) develop and can get progressively worse. Hearing and vision loss also develops during the later stages of Friedreich's ataxia in many individuals. Other symptoms include palpitations, chest pain and shortness of breath. These symptoms are the consequence of various forms of heart disease that often accompany Friedreich's ataxia, such as myocardial fibrosis (formation of fiber-like material in the muscles of the heart) hypertrophic cardiomyopathy (enlargement of the heart), heart rhythm abnormalities, heart block (impaired conduction of cardiac impulses within the heart) and cardiac failure. [5]

About 20 percent of people with Friedreich's ataxia develop carbohydrate intolerance and 10 percent develop diabetes[6]. Within 10 to 20 years after the appearance of the first symptoms, it progresses to a wheelchair is required for mobility and in advanced stages of the disease persons may become completely disabled. Friedreich's ataxia can cause death or shorten life expectancy; heart disease is the most common cause. However, in some people with less features of Friedreich's ataxia living more than sixty years. [6]

CASE DISCUSSION

A 25-year-old male patient admitted in a general medicine with the chief complaints of breathlessness and pedal edema since 10 days and he was previously treated for upper respiratory tract infection. History of fever with titubation for one month observed at the age of six years. The patient was swaying to the right associated with curvature of the spine. These symptoms progressed slowly and then noticed to have difficulty in lifting both upper and lower limbs simultaneously in both proximal and distal region. Difficulty in turning in bed, deterioration of vision since last three years, presently only able to appreciate light. He was found to have high sugar level since last year. Past medical history reveal that known case of DM and dilated cardiomyopathy seeing as one year.

His family history reveal that, elder brother had a similar complaints and the symptoms started at 14 years of his age. Miliaria rubra, Speech dysarthria, higher motor functions, Low volume pulse with irregularities, generalized weakness of all limbs were observed through systemic examination. Immediate and recent memories are present. Vitamin E deficiency observed in the CBC. FBS blood sugar is elevated. SGOT (89 U/L), SGPT (92 U/L) and alkaline phosphatase (165 U/L) levels are increased. LVH & RVH observed in the ECG. In Echo, Mild MR with moderate TR, mild global hypokinesia of left ventricles and mild LVEF of 45 % observed. The thickened gallbladder wall, right pleural effusion and minimal assets were reported in the USG. The speed in which nerves transmit the impulses were observed in the EMG. Molecular genetic testing done already for this patient in a private organization. The test result shown that Autosomal recessive inheritance and he was diagnosed as genetic ataxia.

In this case, first he is treated symptomatically took after by exercise based recuperation. Cell reinforcement drugs like, vitamin E (15 mg), coenzyme q10 (150 mg) and Idebenone (120 mg/day) given to defer malady movement. Drug to

bring down the glucose T. Met SR 1gm and for coronary illness T. Envas 2.5 mg was recommended for decreasing the co-morbidities. Surgery is favored to correct bony deformities. He was improved following 17 days of treatment and the patient was discharged on request. He was advised to go for a routine eye check-up and normal physiotherapy and language instruction for enhancing their intellectual capacities.

DISCUSSION

Idebenone therapy used more than a decade for the treatment of Friedreich's ataxia. At present, several studies have assessed the influence of therapy on neurologic or cardiac function. The effect of intermediate-dose Idebenone (20 mg/kg/d) on quality of life and neurologic function was assessed in a recent study by Brandsema *et al*. [7]

Coenzyme Q is an antioxidant that can buffer the free radical formation that is induced by excess mitochondrial iron. A combined coenzyme Q and vitamin E therapy has been used in a study of 10 patients with slowing of the progression of certain clinical features and a significant improvement in cardiac function. Experimental studies are under pipeline to assess the effect of coenzyme Q derivatives in decreasing the toxicity of iron in mitochondrial structures.

CONCLUSION

At present there is no cure or compelling treatment for Friedreich's ataxia. In any case, the side effects and related entanglements can be dealt with legitimately in FA people to keep up the ideal working to the extent that this would be possible. Specialists can recommend medicines to treat diabetes, pulmonary and heart issues. Supports or surgery will be recommended for adjusting the orthopedic issues, for example, foot deformations and scoliosis etc. Physical treatment may help to arms and legs for normal activity. Advances in understanding the hereditary qualities of friedreich's ataxia are prompting achievements in treatment. Additionally, examines expected to point the medicines for Friedreich's ataxia. Genetic testing is essential for legitimate clinical finding, and can aid in prenatal diagnosis and determining a person's carrier status. Psychological and counseling may help to the influenced people and their families to make do with the illness. A primary care physician can screen people for complications such as heart disease, diabetes and scoliosis, and can refer individuals to specialists such as cardiologists, physical therapists, and speech therapists to help deal with some other associated issues. Counselling centers are also available in number of private organizations. These organizations can recommend ways to network and converse with FA patients or their families. They can also provide access to understanding registries, clinical trials data, and other valuable assets.

ABBREVIATIONS

CBC: Complete blood count
Hb: Heamoglobin
RBS: Random blood sugar
SGOT: Serum glutamate oxaloacetic transaminase
SGPT: Serum glutamate pyruvate transaminase
ECG: Electrocardiogram
USG: Ultra sonography
EMG: Electromyography
LVH: Left ventricular hypertrophy
RVH: Right ventricular hypertrophy
MR: Mitral regurgitation
TR: Tricuspid regurgitation

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