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A Rare Case of an Atypical Friedreich's Ataxia

Case Report

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Introduction

Friedreich's ataxia is one of the most common causes of young onset ataxia. It is a degenerative ataxia initially described by Nicolaus Friedreich, as a clinical syndrome characterized by gait ataxia, incoordination, peripheral neuropathy, absent reflexes, abnormalities in eyes movement, pes cavus, scoliosis, cardiomyopathy, and diabetes mellitus.[1] It is an autosomal recessive disorder, with disabilities usually starts from second decade. Patients suffering from this disease dies at early age due to cardiomyopathy and heart failure. Friedreich's ataxia is due to GAA repeats in long arm of chromosome 9 that affects frataxin gene.[2] Harding, in 1981,described typical form of Friedreich's ataxia with essential criteria such as onset of symptoms before 25 years of age, progressive ataxia of limbs and gait, absent knee and ankle jerks, reduced motor wave conductions, extensor plantar reflex, and onset of dysarthria after five years of disease onset.3 Additional criteria included are pyramidal signs in both limbs, scoliosis, hammer toe, pes cavus, absent reflexes in upper limbs, and abnormal ECG.[2] The MRI reports in the early stages may not demonstrate obvious cerebellar atrophy, but shows cervical spinal cord atrophy. Late stage of the disease will have marked cerebellar atrophy in MRI scans. Studies have reported red flags for excluding the possibility of a diagnosis of Friedreich ataxia, which include prominent cerebellar atrophy, preserved sensory action potential, and mental retardation.[4]

Literature has arbitrarily subdivided Friedreich ataxia based on the delayed age of onset into late-onset (25-39 years) and very late-onset Friedreich ataxia (>40 years).[5] Late-onset cases found to have atypical features including preserved deep tendon reflexes or spasticity with hyperreflexia.[6] Atypical phenotypes of Friedreich's ataxia also have been described in the literature. Schulz et al (2009) listed out the recessive ataxias with similar characteristic features such as ataxia with vitamin E deficiency, ataxia with oculomotor apraxia, and autosomal-recessive spastic ataxia of Charlevoic-Saguenay, which can be considered for differential diagnosis.[7] Here we describe an atypical phenotype presentation of Friedreich's ataxia with retained reflexes.

Case Report

A 34-year-old male, born of second-degree consanguineous marriage, presented with history of unsteadiness in walking noticed at the age of 16 years in the form of swaying to both sides while walking. The symptoms had insidious onset and was gradually progressing. Five years later, patient had sensory symptoms in the form of decreased pain and temperature perception in the lower limbs. The patient also reported to have history suggesting of wash-basin symptoms and double vision. At the same time, patient was diagnosed with diabetes mellitus and was given insulin injection. Further medical evaluation also detected the presence of cardiomyopathy. Gradually, patient had difficulty in speech in the form of articulating words syllable-by-syllable. Patient also had stiffness of both lower limbs, which progressed to an extent that lower limbs were very stiff with scissoring of legs, and he was not able to stand or walk without support. He was almost bedbound after one year, even requires assistance for sitting on bed. The family history revealed similar pattern of symptoms for his paternal uncle.

On evaluation, knuckle pigmentation, hammer toe, pes cavus and scoliosis were identified on general examination. The higher mental functions were found to be normal. Cranial nerve examination revealed nystagmus and square wave jerks. The muscle tone was increased in both lower limbs. However, the ankle jerks were absent while all other tendon reflexes were present. The plantar reflexes hadextensor

response bilaterally, suggesting involvement of corticospinal tract. Pain, touch, vibration, and position sense were impaired bilaterally. Further evaluation identified bilateral impairment in finger-to-finger and finger-to-nose test, and the presence of dysdiadochokinesia and rebound phenomenon, suggestive of cerebellar involvement. There was cerebellar scanning speech, nystagmus, and square wave jerks. Tandem gait could not be elicited as patient could not stand or walk.

On routine investigation, random blood sugars were high. The ECG recordings showed T-inversion in anterior and inferior leads. The ECHO test results reflected hypertrophic cardiomyopathy. The nerve conduction study revealed bilateral upper limb and lower limb axonal neuropathy. Ophthalmological and ENT examinations were unremarkable.

MRI Brain scans showed cerebellar atrophic changes and cervical spinal canal narrowing (Figure 1). Friedreich's ataxia mutational analysis was done for the patient by real time PCR method which revealed homozygous expansion of GAA repeats (> 65 repeats) in the frataxin gene (Figure 2). Thus, patient had a definitive diagnosis of atypical Friedreich's ataxia, with preserved reflexes.

Patient was treated with insulin to control blood sugar and diazepam to reduce spasticity. In view of cardiomyopathy with severe LV dysfunction, furosemide and spironolactone were prescribed after cardiologist opinion. Patient also received in-patient physiotherapy, and was discharged at request after 1 week.

Discussion

Friedreich's ataxia is considered as the most common autosomal recessive ataxia. [8] The neurological features reported in typical form Friedreich's ataxia include gait ataxia, limb ataxia, weakness and wasting which is prominent in the lower limbs, areflexia, sensory loss, abnormalities of the eye movements, dysarthria, dysphagia, auditory neuropathy, and sphincter disturbances.[2] Late stages of the disease reported to have marked cerebellar atrophy.

Atypical phenotypes of Friedreich's ataxia as reported in the literature are Late Onset Friedreich's ataxia (LOFA), Very Late Onset Friedreich's Ataxia (VLOFA), and Friedreich's ataxia with retained reflexes.[9]The reported patient also had severe spasticity, and retained deep tendon reflexes, suggesting atypical phonotype of

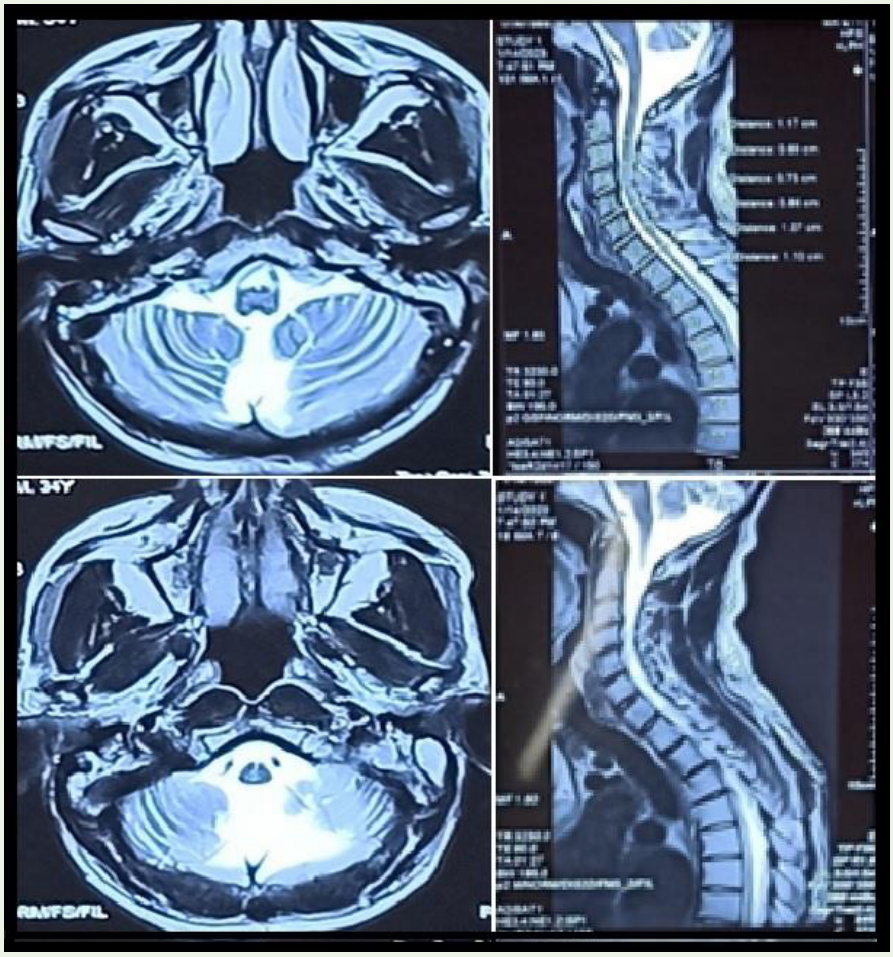

Figure 1: MRI scan findings

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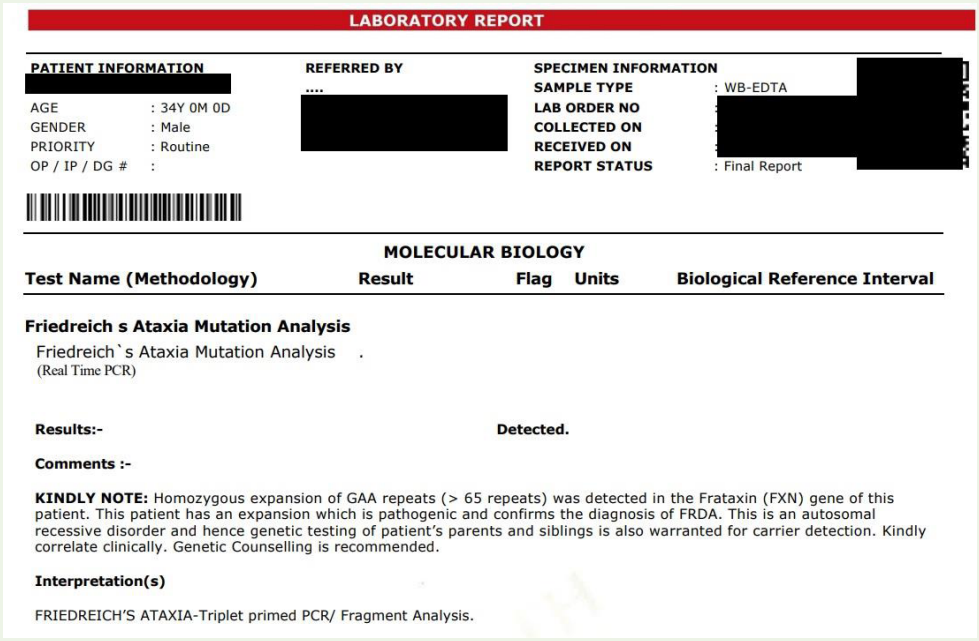

LABORATORY REPORT

PATIENT INFORMATION [redacted]
AGE : 34Y 0M 0D
GENDER : Male
PRIORITY : Routine
OP / IP / DG # :

REFERRED BY
....
[redacted]

SPECIMEN INFORMATION
SAMPLE TYPE : WB-EDTA
LAB ORDER NO
COLLECTED ON
RECEIVED ON
REPORT STATUS : Final Report

MOLECULAR BIOLOGY

Test Name (Methodology)	Result	Flag	Units	Biological Reference Interval

Friedreich s Ataxia Mutation Analysis

Friedreich`s Ataxia Mutation Analysis .
(Real Time PCR)

Results:- **Detected.**

Comments :-

KINDLY NOTE: Homozygous expansion of GAA repeats (> 65 repeats) was detected in the Frataxin (FXN) gene of this patient. This patient has an expansion which is pathogenic and confirms the diagnosis of FRDA. This is an autosomal recessive disorder and hence genetic testing of patient's parents and siblings is also warranted for carrier detection. Kindly correlate clinically. Genetic Counselling is recommended.

Interpretation(s)

FRIEDREICH'S ATAXIA-Triplet primed PCR/ Fragment Analysis.

Figure 2: Friedreich's ataxia mutational analysis results.

Friedreich's ataxia. Klockgether et al., reported 30-40% variance in the presence of spasticity in atypical phenotypes.[10] Literature has also reported atypical variants with cervical cord atrophy,[2] which was also present in this patient.

While studies have reported lower incidence of non-neurological features such as skeletal deformities and cardiac involvement in atypical phenotypes,[11] scoliosis, pes cavus, cardiomyopathy and diabetes were reported in our patient. Cardiomyopathy is reported to be absent in the atypical phenotypes,[2] but the reported patient had hypertrophic cardiomyopathy with abnormal T-wave inversion. Delatycki (2009) reported the progression of Friedreich ataxia to be slow, with a mean time of 36 years between onset and death.[12] Studies have reported treatment strategies with coenzyme Q, vitamin E, Idebenone, and L-carnitine as medical options, which enhances mitochondrial function and act as free radical scavangers.[7]

Our patient presented here had core clinical features of Friedreich's ataxia which was genetically confirmed, and exhibited severe spasticity and retained tendon reflexes, suggestive of an atypical phenotype of Friedreich's ataxia. Knowledge of atypical presentations of Friedreich's ataxia is very important in clinical practice. It will help us differentiate Friedreich's ataxia from other differential diagnoses.

References:

1. Delatycki MB (2000) Friedreich ataxia: an overview. J Med Genet 37: 1-8.
2. Parkinson MH, Boesch S, Nachbauer W, Mariotti C, Giunti P (2013) Clinical features of Friedreich's ataxia: classical and atypical phenotypes. J Neurochem 126: 103-117.
3. Harding AE(1981) Friedreich's ataxia: a clinical and genetic study of 90 families with an analysis of early diagnostic criteria and intrafamilial clustering of clinical features. Brain. 104: 589-620.
4. Moseley ML,Benzow KA, Schut LJ, Bird TD, Gomez CM, et al. (1998) Incidence of dominant spinocerebellar and Friedreich triplet repeats among 361 ataxia families. Neurology 51: 1666-1671.
5. Bidichandani SI, Garcia CA, Patel PI, Dimachkie MM (2000) Very Late-Onset Friedreich Ataxia Despite Large GAA Triplet Repeat Expansions. Arch Neurol 57: 246-251.
6. Indelicato E, Nachbauer W, Eigentler A,Amprosi M,Gothe RM,et al. (2020) Onset features and time to diagnosis in Friedreich's Ataxia. Orphanet J Rare Dis 15: 198.
7. Schulz J, Boesch S, Bürk K, Dürr A, Giunti P, et al.(2009) Diagnosis and treatment of friedreich ataxia: An European perspective. Nature Reviews Neurology 5: 222-234.
8. Lloyd TE, Chaudhry V (2011) Treatment and Management of Hereditary Neuropathies. In: Neuromuscular Disorders: Treatment and Management. Elsevier Pp:191-213.
9. Caron E, Burns D, Castro D, Iannaccone ST (2015) Atypical Presentation for Friedreich Ataxia in a Child. J Clin Neuromuscul Dis17: 13-17.
10. Klockgether T, Zuhlke C, Schulz JB, Burk K, Fetter M, Dittmann H, et al. (1996) Friedreich's ataxia with retained tendon reflexes. Neurology 46: 118-121.
11. Bhidayasiri R, Perlman SL, Pulst SM, Geschwind DH (2005) Late-Onset Friedreich Ataxia. Arch Neurol 62: 1865.
12. Delatycki MB (2009) Evaluating the progression of Friedreich ataxia and its treatment. J Neurol 256: 36-41.

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