MEDICAL CHANNEL

Case Report

INCIDENTAL FINDING OF FRIEDREICH'S ATAXIA IN A GIRL WITH DIABETIC KETOACIDOSIS

** Fahad Khan, ** Sara Ahmed, *** Rauf Memon **** Tahir Ali*

* MBBS, FCPS (Resident of Medicine in Medical Unit II Civil Hospital Karachi), ** MBBS Student (Dow Medical College Karachi) *** (Head of Department, Medical Unit -II Civil Hospital Karachi) **** MBBS (House officer, Medical Unit-II Civil Hospital Karachi)

ABSTRACT

Friedreich's ataxia is an autosomal recessive disorder which is the most common among all hereditary ataxia, prevalant equally among males and females. One out of every 50,000 people of United states are suffering from this. Being a neurodegenerative disorder, it fundamentally affects nerves, neurons and muscles, but mainly damaging nervous and cardiovascular systems and rarely pancreas as well. It is usually presented with uncoordinated limb movements and muscle weakness but occasionally patients with heart manifestations are also seen, varying with the phenotype. Diabetes is an atypical presentation only appreciated among 10% of sufferers. Its age of onset of symptoms is usually 2 years but are frequently evidenced between 5-15 years of age and significantly noticed before 20 years.

Here is a case from medical unit-II of Civil Hospital Karachi which tells about a 16 years old female sufferer. She developed ataxia with limb weakness at the age of 6 and when grew to 12 years she had diabetes. She presented with diabetic ketoacidosis which is the earliest and the most prevalant manifestation of Diabetes Mellitus type 1. Later when further clinical assesments, ECG and labs were conducted, ECG was little impaired but not relatively marked to label cardiomayopathy hence it was an atypical and rare manifestation of friedreich's ataxia with diabetic ketoacidosis directing towards diabetes mellitus.

Key words: Friedreich's Ataxia, Diabetic Ketoacidosis, Neurodegenerative, Frataxin, cardiomayopathy,

Corresponding Author
Dr. Fahad Khan
MBBS, FCPS
(Resident of Medicine in
Medical Unit II
Civil Hospital Karachi)
Khanfahad05@gmail.com
0923212082439
B-51/1, Malir Extension Colony
Karachi, Pakistan
Postal Code 75080

INTRODUCTION

The most common hereditary autosomal recessive ataxia is Friedreich's Ataxia[1] which entertains the frataxin gene mutation on chromosome 9 where among 98% of patients show GAA repeat expansion of frataxin gene which determines the severity of the disease hence greater the size, severe will be the disease[5]. In friedreich's ataxia spinal cord and peripheral nerves are markedly and

progressively damaged results in thinning of nerve fibers. Cerebellum is also degenerated though comparatively less pronounced than spine and nerves but results in unsteady, abnormal movements and deteriorated sensory functions[2,3]. Friedreich's ataxia becomes symptomatic in the first 10-15 years of life, disease manifestation earlier than this age could be the possibility but usually not after 20 years and bounds the patient to wheelchair within 10-15 years of the onset of disease[1,6].

Onset and progression of the disease begin with different signs and symptoms varying in severity from patient to patient. Posterior column neuropathy, peripheral sensory neuropathy, areflexia, progressive limb and gait ataxia (loss of balance and coordination), ascending muscle weakness (begins in the legs and torso and spreads to the arms and hands), ascending loss of vibration and joint position sensations are frequently reported deficits[3,4] while dysarthria, dysphagia, optic neuropathy, auditory neuropathy and scoliosis are unusually seen. Cognitive functions remain intact in friedreich's ataxia[6]. Death either results due to neurological or extra neurological causes of heart and pancreatic loss[7]. Clinically, diagnosis of friedreich's ataxia is based on good history and physical examination to determine the balance difficulty, loss of proprioception, absent reflexes and other neurological signs indicating deficits whereas Genetic testing can confirm friedreich's ataxia.

Being a hereditary disorder, friedreich's ataxia leaves its persistant irremediable marks on the genes of the sufferer and no straight forward treatment so far has arrived to manage it[1]. Cardiac involvement could be the soul reason of mortality so these secondary deficits of this neurodegenerative disorder FA can be treated like managing diabetes and heart problems by drugs, orthopedic defects with braces or surgery, physical therapy to prolong the use of arms and legs, this not only increases life expectancy but markedly improves quality of life as well[2,3]

Case report

A female patient 16 years old, known case of Diabetes Mellitus, came to Emergency department on 20-03-15 with complaints of ? abdominal pain for 1 day, nausea and vomiting for 1 day and ?restlessness for 1 day. According to attendant, the patient was alright 1 day back when she developed sudden, severe, continuous abdominal pain, marked in epigastrium, non-radiating or shifting. It was associated with nausea and vomiting. She was very restless.

She developed Progressive ataxia when six years old. Initially she had unstable gait with in coordination of limb movements and tremors in all extremities, then she had progressive and symmetrical loss of strength and she could only stand and walk with support. By the age of 9, the patient was completely on the bed, unable to stand and walk. She did not have cough, breathlessness, palpitation or chest pain, but she has short positive history of abdominal pain, nausea and vomiting, not associated with complains of heart burn, diarrhea, constipation, hematemesis or melena.

On CNS examination, she was restless, had increased urine frequency, no burning micturition or incontinence was present. At 12 years of age she was diagnosed to have Diabetes mellitus type 1 and she uses insulin R (10 units) for that, her father was also diabetic. She reported to have decreased appetite and sleep, bowel is normal with increased micturition.

On clinical examination:

On general physical examination her vitals are normal and she is well oriented with time, place and person. Jaundice, clubbing and edema are absent, she is mildly dehydrated and moderately anemic.

Systemic examination:

Abdominal examination: no positive finding except mild tenderness.

Respiratory system: chest was clear with NVB .

CVS: S1+S2+0

Musculoskeletal: spine had mild scoliosis, ankle with bilateral pes cavus, and foot has hammer toes

CNS Examination:

Ophthalmic: intact light reflex

Fundus: optic atrophy

Balance and Coordination: scanning speech, dysdiadochokinesia, finger to nose test +ve, heel to shin test +ve.

Motor and Sensory examination: both upper and lower limbs have decreased tone and bulk, both have areflexia, and entensor plantars present, power in upper limb is 4/5 and lower limb is 2/5. Sensory showed impaired vibratory and position sensation.

DISCUSSION

According to Harding's criteria age of onset prior to 25, progressive ataxia, absent deep tendon reflexes and dysarthria are placed in essential criteria. Scoliosis, pyramidal weakness in lower limbs, absent tendon reflexes in arms, impairment of vibration, joint position sense 5 and cardiomyopathy are additional criteria.(2)

This delineated patient was the incidental finding of Friedreich's ataxia although FA appeared at the age of 6 as progressive ataxia followed by unstable gait and uncoordinated limbs but she was kept ignorant. But here she was presented to us in an emergency setup with a short history of fever, abdominal pain, nausea, vomiting and restlessness for one day for which she was managed conservatively. History revealed that she was a known case of diabetes mellitus type 1 for last 4 years and was taking insulin R (10 units) but not regularly due to its high cost. Further clinical assessment and investigations revealed her a sufferer of friedreich's ataxia presented with diabetic ketoacidosis.

Hebinck J. in his research estimated that diabetes is manifested in only 18% of sufferers whereas 39% of FA affected individuals have impaired glucose tolerance.[9] while a research by Zoran suggested diabetes in 10% and glucose intolerance in 20% of patients.[10] showing occurance of diabetes in vey few of the patient.

When we investigated our patient, her RBS was 493mg/dl, HbA1C 9.66, serum ketones were positive and arterial blood gases suggested diabetic ketoacidosis, first and the crucial most finding of DM type 1. Protein traces with pus cells, yeast cells and leucocytes were positive in Urine D/R along with glycosuria and ketonuria. When isolated, yeast cells were candida tropicalis concluding that this case was an infectious presentation of diabetes mellitus with diabetic ketoacidosis.

Our patient was an early onset case of friedreich's ataxia as she developed progressive ataxia, unstable gait, incoordinated limb movements and tremors in all extremities when 6 years old and was wheelchair dependant at the age of 9. Jasvinder in his research reported loss of ambulation usually occurs at 15 years of age and 95% affected people are wheelchair dependant by the age of 45 years.[1] which she exhibited quite early. On her physical examination, she had mild kyphosis, mild scoliosis, high arched palate bilateral pes cavus and hammer toe. Parkinson at el in his research mentioned a marked worsening in condition of patients with early onset friedreich's ataxia and they may have more non-neurological characters like diabetes, cardiomyopathy, scoliosis and pes cavus.[11]

Her further neurological examination revealed reduced tone and muscle bulk of both upper and lower limbs. In lower limbs areflexia, markedly reduced power and extensor plantars were present , while upper limbs have intact reflexes. Pain and temperature sensations were intact in both limbs with impaired vibration and position in lower limbs. Loss of joint position and vibration senses, absent tendon reflexes in the legs and extensor plantar responses are labelled as cardinal features of FA by Jasvinder.[1]

Her ophthalmic examination highlighted optic atrophy on fundus. Because friedreich's ataxia involves cranial nerves hence hearing loss and visual disturbances(optic atrophy or nystagmus) are common.[5] Her coordination was mutilated which is evidenced as one of the symptoms of FA.[4] Considering multifocal atrial tachycardia results in hypertrophic cardiomyopathy in FA[12] her ECG was conducted showing T and ST wave changes with left axis deviation. According to Tsou et al Cardiac causes could be fatal in 60% of the cases.[13]

CONCLUSION

Friedreich's ataxia is the most common of all the ataxia but diabetic ketoacidosis is its rare complication. No permanent treatment can put this disease to the end because no therapeutic measures can modify the neurological deficits and mutated genes.

Informed Consent:

Written informed consent was obtained from the patient for the publication of this case report.

Conflict Of Interest:

There is no conflict of interest among authors in this case report.

REFERENCES

1. "Friedreich's Ataxia Fact Sheet," NINDS. Publication date September 2010. NIH Publication No. 10-87
2. Collins A; Clinical neurogenetics: friedreich ataxia. Neurol Clin. 2013 Nov; 31(4):1095-120. doi: 10.1016/j.ncl.2013.05.002
3. Special report, In Focus: Friedreich's Ataxia, written in December 2010 in MDA, outlines the latest findings in Friedreich's ataxia (FA)
4. patient.co.uk/doctor/friedreichs-ataxia friedreich's ataxia from patient's plus. Patient Plus articles are written by UK doctors and are based on research evidence, UK and European Guidelines.
5. *Peter Gibilisco, research fellow, patient* 1*, Adam P Vogel, senior research,fellowBMJ* 2013; 347(Published 03 December 2013).
6. Martin B Delatycki, MBBS, FRACP, PhD[1,2,3] and Louise A Corben, BAppSci (OT), MSci[1] J Child Neurol. Author manuscript; available in PMC 2013 Sep 1.Published in final edited form as: J Child Neurol. 2012 Sep; 27(9):1133–1137.
7. Friedreich's ataxia: a guide for the medical profession; Ataxia UK
8. Hebinck J., Hardt C., Schöls L., Vorgerd M., Briedigkeit L., Kahn R.C., Ristow M. Heterozygous expansion of the GAA tract of the X25/frataxin gene is associated with insulin resistance in humans. Diabetes 2000; 49: 1604-1607.
9. Zoran Gucev*, Velibor Tasic, Aleksandra Jancevska, Nada Popjordanova, Svetlana Koceva, Marija Kuturec, Vesna Sabolic Faculty of Medicine Skopje, St. Cyril and Methodius University, 50 Divizija BB, 1000 Skopje, Macedonia
10. J Neurochem. 2013 Aug;126 Suppl 1:103-17. doi: 10.1111/jnc.12317. Clinical features of Friedreich's ataxia: classical and atypical phenotypes. Parkinson MH[1], Boesch S, Nachbauer W, Mariotti C, Giunti P.
11. Kolek M[1], Mrózek V, Schenk P.[Cardiac manifestations of Friedreich's ataxia].[Article in Czech] Cas Lek Cesk. 2004;143(1):48-51
12. Tsou AY, Paulsen EK, Lagedrost SJ, Perlman SL, Mathews KD, Wilmot GR, Ravina B, Koeppen AH, Lynch DR. Mortality in Friedreich ataxia. J Neurol Sci.2011;307:46–49.
13. Koeppen AH. Friedreich's ataxia: pathology, pathogenesis, and molecular genetics. J Neurol Sci. 2011;303:1–12.