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A CASE OF WOLFRAM SYNDROME - CASE REPORT

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Abstract: **Wolfram syndrome is a rare autosomal recessive disorder caused by mutations in WFS1, a gene implicated in endoplasmic reticulum and mitochondrial function. It is characterized by insulin-requiring diabetes mellitus and optic atrophy. An older name for the syndrome is DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness). A 17 year old male patient, a know case of diabetes mellitus type I diagnosed 11 years back and significant for optic atrophy, diagnosed at age 11 which progressed to severe visual impairment over the following 6 years.**

This study point up the need for careful evaluation of such cases having insulin dependent diabetes mellitus and optic atrophy. Wolfram syndrome affects different organs and systems in the body. Thus, multidisciplinary care by physicians and healthcare professionals from a range of disciplines is required. Careful clinical monitoring and supportive care can help relieve the suffering of patients and improve their quality of life.

Keywords: **Wolfram syndrome; Optic atrophy; Diabetes mellitus; Deafness.**

I. INTRODUCTION

Wolfram syndrome is a inherited condition initialy described in 1938 as a combination of juvenile-onset diabetes mellitus and optic atrophy. An older name for the syndrome is DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness). Minimal criteria for establishing the diagnosis are diabetes mellitus and optic atrophy. Diabetes insipidus, sensorineural deafness, urinary tract atony, ataxia, mental retardation, peripheral neuropathy and psychiatric disorders are additional findings present in most of patients.[1]

Diabetes mellitus is typically the first symptom that occurr around age 6. Nearly everyone with Wolfram syndrome who develops diabetes mellitus requires insulin replacement therapy. Optic atrophy is often the next symptom to appear, usually around age 11. The initial signs of optic atrophy are loss of color vision and side (peripheral) vision. Then after a while the vision problems get worse, and people with optic atrophy are usually blind within approximately 8 years after signs of optic atrophy first began.[2]

There are two types of Wolfram syndrome with many overlapping features, this two types are differentiated by their genetic cause. In addition to the usual features of Wolfram syndrome, individuals with Wolfram syndrome type 2 have stomach or intestinal ulcers and excessive bleeding after an injury. The tendency to bleed excessively combined with the ulcers typically leads to abnormal bleeding in the gastrointestinal system. People with Wolfram syndrome type 2 do not develop diabetes insipidus.[2]

II. CASE REPORT

A 17 year old male patient, a know case of diabetes mellitus type I diagnosed 11 years back, presented to a government hospital. Patients RBS (Random blood sugar) was 273 mg/dl during admission, then he was given injection insulin glargine (0-0-20units) along with injection insulin lispro (10-10-10units) and blood sugar level was brought down to 75mg/dl. Family history, parents are not diabetic but his grandparents are diabetic. On examination, his BMI was 17.8 kg/m^2 . His bystander said he was having low BMI from past 17 years. His past medical history was significant for optic atrophy, diagnosed at age 11 which progressed to severe visual impairment over the following 6 years. Fundus

examination showed no sign of diabetic retinopathy. From last month he frequently complains about hearing problem and feels agitated. An audiologic examination revealed that the patient has neurosensory deafness. Magnetic resonance imaging (MRI) was taken of the brain and lumbar spine was normal. Patient complaint about frequent urination. Renal, hepatic, and thyroid functions were normal. Urea: 31 mg/dL, creatinine: 1 mg/dL, creatinine clearance = 84 mL/min, calcium: 10.6 mg/dL, phosphorus: 3.7 mg/dL, sodium: 139 mg/dL, potassium: 4.8 mg/dL, hemoglobin A1c: 13.4%, alanine transaminase: 32 IU/L, aspartate transaminase: 35 IU/L, alkaline phosphatase: 219 U/L, total bilirubin: 1.0 mg/dL, direct bilirubin: 0.4 mg/dL, T4: 9.1 ng/dL, T3: 136 ng/dL, thyroid-stimulating hormone: 2.8 mU/L

III. DISCUSSION

Wolfram syndrome is a progressive autosomal recessive neurodegenerative disorder.[3] Hallmarks of the syndrome are diabetes mellitus, which is usually the first sign of the disease (median age at diagnosis, 6–15 years), and optic atrophy (median age at diagnosis 11 years). Optic atrophy in a diabetic patient necessitates intravenous pyelography and audiometry.[3] In our patient the majority of symptoms became manifest by the first and second decade of life and a correct diagnosis had been made when he was 11 years old.

Optic atrophy, a consistent finding in all patients, occurs at an average age of 11 years [5]. At the age of 11 years our patient started to have progressive visual loss and found to have optic atrophy which is not related to diabetes mellitus because there was no evidence of diabetic retinopathy.

Deafness in Wolfram syndrome is commonly seen in high frequency, symmetric hearing loss, usually detected in the second or third decade with a relatively slow rate of deterioration. [6] ,[7] In our patient, he complained about hearing problem around the age of 17.

There is no definitive treatment for Wolfram syndrome . Diabetes mellitus is managed with insulin, and vasopressin for diabetes insipidus. there is no treatment for loss of vision. Regarding the deafness, hearing aids can help. Neurogenic bladder may be treated by intermittent catheterization and some medications like oxybutynin .[6]

IV. CONCLUSION

Wolfram syndrome should be considered when the diabetes patients present with optic atrophy. Clinical suspicion at an early stage is important for prompt diagnosis and proper management. Renal failure is one of the important causes of death in wolfram syndrome , a careful assessment for urinary tract abnormalities and urinary infections are recommended.[5] Wolfram syndrome affects different organs and systems in the body. Thus, multidisciplinary care by physicians and healthcare professionals from a range of disciplines is required. careful clinical monitoring and supportive care can help relieve the suffering of patients and improve their quality of life.

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