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Wolfram syndrome: A case report

Alireza Eskandarifar[1], Banafsheh Sedaghat[2], Somayeh Janany[2], Mozhgan Hosseiny[3], Alireza Gharib[4]

1 Assistant Professor, Department of Pediatrics, School of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran
2 Resident, Department of Pediatrics Diseases, School of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran
3 MSc Student, School of Management and Medical Informatics, Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
4 Deputy of Research, Kurdistan University of Medical Sciences, Sanandaj, Iran

Case Report

Abstract

Wolfram syndrome (WFS) is a rare disease inherited as an autosomal dominant trait. Type I diabetes mellitus and optic atrophy are the main symptoms of the disease. It is also known as DIDMOAD syndrome due to the association of diabetes insipidus, diabetes mellitus, optic atrophy, and deafness. WFS may be associated with other disorders such as kidney failure, gonadal atrophy, and mental and behavioral disorders. This report is about a 14-year-old teenager who had suffered from vision loss and cataracts when he was 4 years old. At the age of 7 he has been diagnosed with type I diabetes mellitus due to polyuria and polydipsia. At the age of 12 he developed diabetes insipidus, neural hearing loss, urinary incontinence and bilateral hydronephrosis, neurogenic bladder, and increased blood pressure. Physicians should think of this disease and recommend genetic counselling before marriage.

KEYWORDS: Wolfram Syndrome, DIDMOAD, Optic Nerve Atrophy, Hearing Loss, Diabetes

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Introduction

Wolfram syndrome (WFS) is a rarely inherited disease that was first reported in 1938.[1,2] Pedigree analysis has shown that it is inherited through autosomal recessive.[3,4] WFS1 gene that is located on the short arm of the chromosome 4P16.1 is responsible for the disease that is seen in 90% of the patients.[5,6] Its frequency varies in different parts of the world and is about one in 500,000 children. In the UK its frequency is estimated about 1 in 770,000.[5,6] The first and most prominent clinical manifestation is diabetes mellitus and optic atrophy which is usually occurs in the first decade of life.[4] In the course of the disease, most patients suffer from diabetes insipidus and sensorineural hearing loss; hence, it is called diabetes insipidus, diabetes mellitus, optic atrophy, and deafness syndrome (DIDMOAD). In addition to these core symptoms, other disorders such as early cataracts, abnormal optic reflux, nystagmus, renal disorders and neurological complications in the form of ataxia, mental disorders and behavioral and gonadal atrophy could be marked in some cases.[6,7] Most patients eventually develop these complications and 65% of patients die before the age of 35 years.[7-10] Nevertheless, this disease is still not well known.

Corresponding Author:
Alireza Gharib
Email: gharibalireza@yahoo.com

Case Report

The patient was a 14-year-old boy who was admitted to the pediatric ward due to diabetes mellitus. The parents were healthy with no

family relationship. In the initial examination, the patient had decreased vision and hearing loss and urinary incontinence. The patient referred to the optician when he was 4 years old due to bilateral visual loss and went under surgery due to cataract. However, the cause of the premature cataract was not investigated further. At the age of 7, the patient was investigated due to polyuria, polydipsia, and urinary incontinence. Then insulin therapy started for him after the diagnosis of type I diabetes mellitus. However, polyuria and polydipsia continued despite insulin therapy. Water deprivation test was done due to low urine specific gravity (SG) and clinical suspicion of diabetes insipidus and after confirming the diagnosis Minirin was started. In recent hospitalization, patient's blood pressure in several assessments was 160/90 mmHg.

In laboratory examination, results blood urea nitrogen = 42, creatinine = 2, and ratio of protein to creatinine in a random urine was about 0.5. Patient glomerular filtration rate was calculated at about 52 using Schwartz formula.

Ultrasound results showed thickened bladder wall revealing coarse echoes of the trabeculae and bladder residual volume was about 150 cc. The patient underwent voiding cystourethrogram to evaluate hydronephrosis with bilateral reflux and distended bladder, the bladder wall was thickened and irregular with bladder diverticulum resulting the improper bladder emptying ending in the diagnosis of neurogenic bladder. Eye examination by an ophthalmologist showed bilateral nerve atrophy. The patient went under tympanometry and audiometry to assess hearing loss. Audiometric pure tone audiometry results showed high frequency neural hearing loss; however, tympanometry results were normal. According to the finding's diagnosis of WFS considered for the patient. Kidney failure in a patient could be related to diabetic nephropathy aggravated by neurogenic bladder and shifting secondary to reflux. Patient's blood sugar and polyuria controlled using insulin and 1-desamino-8-D-arginine vasopressin (DDAVP) spray. Then, the patient discharged after prescribing terazosin and oxybutynin and bladder catheterization training.

Discussion

WFS is an autosomal dominant disorder. The disease is more common in areas of the world where familial marriage is more common. Its prevalence in the world is 1 in 68,000. The first and most prominent clinical manifestation of this disease is diabetes mellitus at an early age. The age of disease onset varies from 3 to 16 years with an average of 6 years. However, our patient age was 4 years.[1,2,7] Diagnosis of WFS in adolescents is possible at an early stage after manifestation of diabetes mellitus and optic atrophy. Premature cataracts have been reported in 29% of the patients as well.[6] In our case, the first manifestation of the disease was occurrence of cataract at the age of 4. Other ocular disorders such as diabetic retinopathy, abnormal light reflex, and nystagmus may also occur.[6] Patients with a wide range of urologic disorders such as reflux and urinary bladder dysfunction have been reported. Urologic disorders may occur in 58% of patients aged 25-10 years with an average age of 20 years.[6] Our case had neurogenic bladder and vesicoureteral reflux. Hearing impairment in WFS is progressive and can be another symptom of the disease.

Neural hearing loss in 60% of the cases is in the high frequencies and occurs in the second and third decades of life with an average age of 16 years. In our patient, tympanomerty was normal, and audiometry results showed hearing loss in high frequencies.[11] In the third and fourth decades with an average age of 30 years, neurological symptoms appear in 62% of patients. The most common symptoms of nerve involvement can be ataxia, loss of smell, dysarthria, hemiparesis, seizures, and nystagmus.[12] In 25% of the cases mental disorders such as psychosis, mood disorders, and depression may be seen. This mental and

physical disorder is progressive and may result in the midlife mortalities.[4,6,13]

Conclusion

Diabetes mellitus is an early manifestation of WFS and late diabetes occurs in the second and third decades of life. Therefore, in cases of diabetes mellitus with early abnormalities such as visual disturbances, hearing disorders, and renal disorders, it is suggested to consider WFS. In cases where there is no family history of diabetes and especially when it is associated with hearing and vision problems or when diabetes autoantibodies are negative one must think of special monogenic forms of the disease. Also, in different parts of the world where consanguinity is more common, such as Iran and other Middle East countries, physicians should consider the disease and recommend genetic counseling before marriage.

Conflict of Interests

Authors have no conflict of interests.

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