CASE REPORT

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Bilateral Optic Nerve Atrophy Case Report

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Abstract

Wolfram syndrome, also known as DIDMOAD or juvenile onset diabetes mellitus, optic nerve atrophy, diabetes insipidus, and deafness, is a genetic neurological condition. This case report provides a description on the first instance of Wolfram syndrome in a Saudi family, which manifested as proliferative diabetic retinopathy and a powder-like cataract, among the other unusual ophthalmological findings. This case involved a 27-year-old Saudi woman with bilateral optic nerve atrophy who was first diagnosed with diabetes mellitus at the age of 8 years. At the age of 18, bilateral optic nerve atrophy was identified. At the age of 27, diabetes insipidus and hearing loss were verified. There were no signs of renal, neurological, or psychiatric issues. Atypical ophthalmological traits were examined and addressed in this study. Any individual with bilateral optic nerve atrophy and insulin-dependent diabetes mellitus within the first 30 years of life should be evaluated for the possibility of Wolfram syndrome. Microvascular diabetes is an incredibly rare complication of Wolfram syndrome. Early diagnosis, treatment, and prevention of severe consequences can result in improved survival rates and quality of life.

Keywords: Atrophy, optic nerve, wolfram syndrome, Saudi Arabia

Introduction

Wolfram made the first observation in 1938, and Wagener later explained it. A complicated, uncommon, autosomal recessive neurological illness, Wolfram syndrome (MIM222300) is inherited. It is also known as DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness) and is defined by juvenile onset non-immune insulin dependent diabetes mellitus, progressive bilateral optic nerve atrophy, and sensorineural hearing loss.[1,2,3] Urinary tract, neurological, reproductive, and psychological problems may be linked to Wolfram syndrome. This disease's pathophysiology is still a mystery.[1,2] The wolfram syndrome mutant gene (WFS1) has been located on chromosome 4p 16.1, however there is evidence of locus heterogeneity and mutations in mitochondrial genes in a small number of documented cases.[4,5] In the UK, 1/770.000 was reported as the prevalence rate.[6] According to several publications, the proportion of individuals with a full Wolfram syndrome varies between 13% and 53%. Less than 8% of the 300 patients described in the literature from all around the globe had diabetic retinopathy as a side effect of wolfram syndrome.[1] There are, however, just a few sources that describe the relationship of cataracts with this disease. This case report describes the first case of Wolfram syndrome in a Saudi family, which manifested as proliferative diabetic retinopathy and a powder-like cataract, among other uncommon ophthalmological findings. The aim of this case report was to report the case of Saudi female patient who was diagnosed with diabetes mellitus, bilateral optic nerve atrophy, and hearing loss.

Case

A 27-year-old Saudi woman with bilateral optic nerve atrophy was sent to the eye clinic at King Abdullah Medical City. Her medical history showed that both of her eyes' visual acuity had gradually declined beginning at age seven, and at age eighteen, she had been identified as having bilateral optic nerve atrophy. She was first diagnosed with insulin-dependent diabetes mellitus when she was eight years old. Despite using insulin, she frequently had uncontrolled

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blood sugar. At the age of 20, she disclosed a history of polyuria and polydipsia, but she didn't seek medical attention. Her consanguineous parents' good family history was crucial. Her older sister, 35, has had insulin-dependent diabetes since she was 10 years old. Later, she experienced hearing and vision problems. Her younger sister and brother, however, were in good health. Her greatest corrected visual acuity was found to be counting fingers in both eyes during assessment. At the age of twenty-seven, she was legally blind and had the maximum corrected visual acuity of counting digits at a distance of two meters. Clinical and biochemical tests, including urine and serum osmolality measurements and the water-deprivation test, all supported the diagnosis of diabetes insipidus of central origin. Her eldest sister had a significant familial history of hearing loss. Our audiogram, which was typical for hearing loss at medium to high frequencies, revealed sensorineural hearing loss. The intraocular pressure in the right eye was 14 mmHg, whereas the intraocular pressure in the left eye was 16 mmHg. RAPD was not found in either of the eyes. Slit lamp examination revealed cataracts that resembled powder during lamellar tiny spots opacity in both lenses. A fundus examination revealed a bilateral pale disc that was a sign of optic atrophy. Additionally, the macula in both eyes displayed some hard exudate, a microaneurysm, and hemorrhage as a result of diabetic retinopathy. Only the right eye had proliferative diabetic retinopathy, which caused preretinal hemorrhage and other neovascularization. The patient received a thorough radiological and laboratory assessment, which included normal US scans of the kidney and bladder as well as the kidney and orbit on CT and MRI. According to osmometer measurements, urine's osmolality was low (170 mosm/kg) and serum's was high (305 mosm/kg). The results of the water-deprivation test supported central diabetic insipidus. Analyses of the urine revealed microalbuminuria. An audiogram with moderate to severe sloping and symmetric sensorineural hearing loss in both ears, with a preference for medium to high frequencies, was found. In this case, no signs of renal, neurological, reproductive, or psychological problems were found. Regarding her older sister, a fundus exam revealed bilateral pale optic discs indicative of optic atrophy and no changes associated with diabetic retinopathy. She wasn't accessible for a second assessment, despite our suspicions that she could have Wolfram syndrome.

This study used de-identified data and was considered exempt from human protection oversight by the institutional review board. Informed consent to participate was obtained from the patient.

Discussion

In the early phases of the illness, wolfram syndrome diagnosis is not usually straightforward. The possibility of juvenile onset diabetes mellitus and an atrophying optic nerve is the suspicion. According to previous literature [2], these two characteristics are rather stable (99% for DM and 97.5% for optic atrophy), in contrast to the other signs and symptoms, which are highly varied in terms of age of start and severity. Before the age of ten, non-immune type 1 diabetes usually manifests as Wolfram syndrome. Diabetes mellitus linked with wolfram syndrome has the same clinical characteristics as type 1 diabetes mellitus. However, the main distinction between autoimmune diabetes and typical type 1 diabetes mellitus is that the former lacks a particular immune or genetic component. The fact that glycemic control is simpler to achieve in wolfram syndrome is another significant distinction from type 1 diabetes mellitus as a whole [1]. Except in extremely rare circumstances, wolfram syndrome does not typically exhibit any symptoms of diabetic retinopathy.[7,8] Diabetic retinopathy was uncommon and, when it was present, proceeded more slowly than anticipated in patients with long-term diabetes mellitus (>15 years). The frequency of diabetic retinopathy in wolfram syndrome was 8%.[7,8] The more manageable nature of diabetes mellitus in wolfram syndrome may have contributed to the previous study's finding that diabetic retinopathy is on the decline [7,8]. There have been reports of a few more severe proliferative retinopathies. Here, we present the case of a patient with wolfram syndrome who was diagnosed 27 years after developing insulin-dependent diabetes at the age of 8. At the age of 27, she experienced preretinal hemorrhage in her right eye as well as proliferative diabetic retinopathy in both of her eyes. She had laser therapy (also known as pan retinal photocoagulation). Optic nerve atrophy, a defining feature of Wolfram syndrome, often began before the age of 15. The average age of the patients was 13.1, with a range of 6 to 30 years.[9-12] Optic atrophy was the first presenting symptom in just 9% of wolfram syndrome patients [1,8]. Optic atrophy often results in a fairly severe vision

impairment, with young adults having visual acuities between 20/200 and 20/400. Total blindness in wolfram syndrome is uncommon, and it takes seven years for considerable vision loss to be considered legally blind. Severe axon loss and demyelination of the optic nerve, chiasm, and tracks are the main causes of blindness. The vision issues in our situation began at a young age of seven. At the age of 18, the patient was identified as having bilateral optic nerve atrophy. She was legally blind at the age of twenty-seven and had the greatest corrected visual acuity of counting fingers at a distance of two meters. Rarely is the occurrence of lens opacity linked to wolfram syndrome mentioned in literature. There are succinct and cryptic statements that fail to identify a specific kind of lens opacity [1]. At the age of 27, we discovered lens opacity in both of our patient's eyes, which was characterized as looking like powder. One instance with the same kind of lens opacity has been documented in the literature.[1,8] Wolfram syndrome does not always include diabetes insipidus, and symptoms typically appear in the second or third decade (between 3 and 40 years old) and are often brought on by central origin abnormalities rather than nephrogenic causes. The atrophy and gliosis of the whole supraoptic and paraventricular neurohypophysaroious system, which results in a deficit in vasopressin, which is responsible for the concentration of urine, was shown by histological and clinical investigations to be the cause of this problem.[10,11,13] This patient's modest polyuria and polydipsia, two signs of diabetes insipidus, first appeared when she was twenty years old. At age 27, she began to experience mild symptoms like polyuria, polydipsia, and nocturia. Clinical and biochemical tests, such as urine and serum osmolality measurements as well as the water-deprivation test, all supported the diagnosis of central origin diabetes insipidus. Due to the fact that it has no impact on voice frequencies, sensorineural hearing loss is often not apparent in adolescents and young adults. When an audiogram revealed severe high frequency loss without any symptoms, as we saw in our instance, it might be a useful diagnostic tool. These individuals' deafness is neurological in nature, affecting the auditory nerve and its central route. Degenerative atrophy of the vestibulocochlear nuclei and inferior colliculi causes a reduction in auditory perception rather than a problem with sound transmission to the nerve.[5,11] The majority of the cases have high frequency hearing loss, which, while it does not affect the ability to hear voices, may have important implications for career counseling.[5]

In this instance, the patient denied having any hearing issues. However, as was mentioned above, she had a strong family history of hearing loss in her older sister. The audiogram in our situation, which was typical for medium to high frequency hearing loss, revealed sensorineural hearing loss. Urinary tract abnormalities, hypogonadism, complications of the central nervous system such ataxia and nystagmus, and mental disorders are prone to develop as people age and should be tested for on a regular basis. In these patients, the median death age is 28 years, and up to 60% of cases pass away by the time they are 35 years old.[9,10] Following brain stem atrophy, central respiratory failure is the primary cause of death. Unfortunately, there is currently no cure for Wolfram syndrome patients to stop the underlying neurodegenerative process. The significant differential diagnoses for wolfram syndrome that need to be ruled out are Friedreich's ataxia, Leber's hereditary optic atrophy, and Behr's optic atrophy.

Bilateral optic nerve atrophy is a pathological disorder characterized by the progressive degeneration of the optic nerves, resulting in the impairment or loss of visual function. The process of establishing a definitive diagnosis encompasses a comprehensive approach that includes clinical evaluation, assessment of medical history, and utilization of several diagnostic techniques such as Visual Field Testing, Visual Acuity Testing, Ophthalmoscopy/ Funduscopy, Optical Coherence Tomography, and Magnetic Resonance Imaging.

In conclusion, anyone who has bilateral optic nerve atrophy and insulin-dependent diabetic mellitus during the first three decades of life should be evaluated for the possibility of Wolfram syndrome. An extremely uncommon consequence of wolfram syndrome is micro vascular diabetes. Improved survival rates and quality of life may result from early diagnosis, treatment, and prevention of major consequences. The comprehensive documentation of the patient's diagnostic process, encompassing the encountered problems in determining the etiology of optic nerve atrophy and hearing loss, can aid healthcare professionals in enhancing their diagnostic methodologies and exploring a wider spectrum of potential causative elements.

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