Wolfram Syndrome (DIDMOAD): A Rare Genetic Neurodegenerative Disorder

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Abstract:

Background:

Wolfram Syndrome is an autosomal recessive neurodegenerative disorder caused by mutations in the WFS1 gene.

Objective:

We report four clinical cases of patients with Wolfram Syndrome to discuss its clinical features, genetic transmission, complications, and the importance of a multidisciplinary approach in managing this condition.

Case Reports:

Case 1: H.A, 24 years old, insulin-treated diabetic for 17 years, polyuropolydipsic syndrome suggestive of diabetes insipidus, decreased visual acuity for 4 years. Fundus examination had shown bilateral optic atrophy associated with pigmentary alterations of the peripheral retina.
Case 2: A 39-year-old woman with a 32-year history of insulin-treated diabetes and bilateral blindness for 20 years presented with polydipsic polyuria symptoms. Suspected Wolfram Syndrome due to early-onset diabetes, family history, and clinical findings. Diagnosis confirmed through papillary atrophy, and hydronephrosis, and improved with desmopressin treatment.
Case 3: A.S., aged 27, insulin-treated diabetic for 20 years, followed for reduced visual acuity since the age of 10, diabetes insipidus on desmopressin for 14 years, secondary enuresis since the age of 8. Pelvic ultrasound showed ureterohydronephrosis with a reduction of the cortical index to 10 mm, and the fundus examination showed optic atrophy.

Case 4: F.S., 23 years old, diabetic for 17 years, insulin-treated since age 6, was followed for diabetes insipidus on desmopressin, a decrease in visual acuity complicated by blindness. The patient had urinary incontinence. Ultrasound showed a very probable neurogenic bladder. The patient died of hyperglycemia with cerebral thrombophlebitis.

Discussion And Conclusion:

Wolfram Syndrome can occur sporadically or in a familial context, following an autosomal recessive mode of inheritance. Mutation of the WFS1 gene on chromosome 4p16.1, coding for the transmembrane protein wolframine, is the main genetic culprit. The typical clinical course of Wolfram Syndrome involves the onset of non-immunological type 1 diabetes in early childhood, followed by diabetes insipidus and sensorineural hearing loss in the second decade of life. Urological disorders generally appear in the third decade. The average life expectancy of sufferers is 30 to 35 years. The management of Wolfram Syndrome presents significant challenges, including sensory deficits, early blindness, and renal failure. Prognosis is influenced by vascular complications associated with diabetes, renal failure, and respiratory problems. A multidisciplinary approach is imperative to meet the complex needs of these patients and offer them a better quality of life.

Keywords:

wolfram syndrome, wolframine, diabetes Mellitus, Optic Atrophy, diabetes insipidus.