Wolfram syndrome: Three cases

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İntroduction: Wolfram syndrome is an autosomal recessive disorder accompanied by diabetes insipidus, diabetes mellitus, optic atrophy and deafness. Mutations in the WFS1 gene are determined in 90% of cases. We present the clinical features of three cases of Wolfram syndrome.

Case 1

History :

14-year-old girl presented with loss of vision

At the age of 3 years
Polyuri - polydipsia
Blood glucose 410 mg/dL
Ketone positivity in urine (++)
→ Diabetes mellitus Type 1

At the age of 8 years
Blood glucose normal
Polyuri - polydipsia
Low urinary specific gravity
→ Water Deprivation test
→ Central Diabetes İnsipidus
→ Desmopressin (nasal spray therapy)

At the age of 8 years → Blurred vision
→ Cataract was determined in the right eye
→ Cataract surgery
→ Optic atrophy was determined at fundus examination following cataract surgery

Family History

No consanguinity was identified between the parents
A brother had died from diabetic ketoacidosis at the age of 4 years
A 24-year-old sister had been diagnosed with type 1 diabetes mellitus

Physical Examination:

Weight: 38 kgs (- 2.3 SDS) Height : 145 cm (-2.3 SDS)
Puberty Tanner stage 3 Blood Pressure 110/60 mmHg
Arthropathy was determined in the fingers

Audiometry: no loss of hearing

Genetic:
Homozygous p.I845N (c 2534T>A) mutation in the WFS1 gene
(The parents were also heterozygous for the same mutation)

Monitoring: HbA1c was between 8% and 9% with multiple insulin therapy and exchange list nutrition

Case 2

History :

7-year-old male patient
Polyuri - polydipsia
Vision was reported to be poor since babyhood

Family History: Parents were second-degree cousins

Physical Examination
Weight: 35 kgs (3.3 SDS) BMI 26.4 kg/m² (3.2 SDS)
Height : 115 cm (-1.2 SDS) Puberty Tanner stage 1
Blood Pressure 100/60 mmHg
Central type obesity, constant nystagmus
Vision was at the light perception level
Bilateral optic atrophy and pigmented retinopathy were observed at fundus examination

Blood glucose 209 mg/dL
ketone positivity in urine (++)
Hba1c 7,5%
→ Diabetes mellitus Type 1

Fundus examination:
- Bilateral optic atrophy (+)
- Pigmented retinopathy (+)

Audiometry: 60 db sensorial loss (+)

Genetic:
No mutation was detected at WFS1 gene analysis
WFS2 mutation in the gene was designed to work

Monitoring: HbA1c was between 7.5% and 8.5% with multiple insulin therapy and exchange list nutrition

Case 3

History :

9-year-old girl

At the age of 3 years – loss of vision

At the age of 8 years
Blood glucose normal
Polyuri - polydipsia
Low urinary specific gravity
→ Water Deprivation test
→ Central Diabetes İnsipidus
→ Desmopressin (nasal spray therapy)

Family History : Unremarkable

Physical Examination
Weight: 26.5 kgs (-0.8 SDS) BMI 16.5 kg/m² (0.1 SDS)
Height : 126.5 cm (-0.5 SDS) Puberty Tanner stage 1

Fundus examination:
- central area was normal
- Periphery - abundant salt and pepper pigmentation
- Total block of transmission (complete blindness) was determined with VEP and ERG

Audiometry: no loss of hearing

Genetic analysis could not be performed

Monitoring: HbA1c 4.8%
Oral Glucose Tolerance Test was normal

	Case 1 / Female	Case 2 / Male	Case 3 / Female
Diabetes mellitus type 1	Yes	Yes	No
Visual defects	optic atrophy, cataract	optic atrophy, pigmented retinopathy, nystagmus	optic atrophy, pigmented retinopathy
Diabetes insipidus	Yes	No	Yes
Hearing loss	No	Yes	No
Neurological and psychiatric problems	No	Yes Mental retardation	No
Short stature	Yes	No	No
Family relationships	No the same village	Yes 1st degree relatives	No
Family history	2 siblings in diabetes mellitus type 1	No	No
Genetic	WFS1 homozigous (p.I845N)	WFS1 : No mutation	No attempt

Table 1. Characteristics of patients with Wolfram Syndrome

Conclusion: Clinical features may differ in presentations of Wolfram syndrome. The syndrome may emerge during monitoring even if not all the features are present concurrently at presentation.

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