Wolfram syndrome: Three cases

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Introduction: 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
  - Polyuria - polydipsia
  - Blood glucose 410 mg/dL
  - Ketone positivity in urine (++)
- At the age of 8 years
  - Blood glucose normal
  - Polyuria - polydipsia
  - Low urinary specific gravity

**Physical Examination:**
- Central diabetes insipidus
- Desmopressin (nasal spray therapy)
- Cataract was determined in the right eye
- 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

**Diabetes mellitus type 1**

**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 7.5% and 8.5% with multiple insulin therapy and exchange list nutrition

### Case 2

**History:** 7-year-old male patient
- Polyuria - polydipsia
- Vision was reported to be poor since babyhood

**Physical Examination:**
- Weight: 35 kg (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

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

**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
  - Polyuria - polydipsia
  - Low urinary specific gravity

**Physical Examination:**
- Weight: 26.5 kg (-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

**Genetic analysis could not be performed**

**Monitoring:**
- HbA1c 4.8%
- Oral Glucose Tolerance Test was normal

### Table 1. Characteristics of patients with Wolfram Syndrome

<table>
<thead>
<tr>
<th>Case 1 / Female</th>
<th>Case 2 / Male</th>
<th>Case 3 / Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus type 1</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Visual defects</td>
<td>optic atrophy, cataract</td>
<td>optic atrophy, pigmented retinopathy, nystagmus</td>
</tr>
<tr>
<td>Diabetes insipidus</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Neurological and psychiatric problems</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Short stature</td>
<td>Yes</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Family relationships</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Family history</td>
<td>2 siblings in diabetes mellitus type 1</td>
<td>1st degree relatives</td>
</tr>
<tr>
<td>Genetic</td>
<td>WFS1 homozygous (p.I845N)</td>
<td>WFS1 : No mutation</td>
</tr>
</tbody>
</table>

**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.