



## Wolfram Syndrome Case With Hypergonadotrophic Hypogonadism: A Novel Mutation

Zeynep Uzan Tatlı<sup>1</sup>, Gül Direk<sup>1</sup>, Merve Nur Hepokur<sup>1</sup>, Nihal Hatipoğlu<sup>1</sup>, Leyla Akın<sup>1</sup>, Mustafa Kendirci<sup>1</sup>, Selim Kurtoğlu<sup>2</sup>

<sup>1</sup>Erciyes University Faculty of Medicine, Department of Pediatric Endocrinology, Turkey / Kayseri

<sup>2</sup>Memorial Hospital, Department of Pediatric Endocrinology and Neonatology, Turkey / Kayseri

### INTRODUCTION

A rare cause of diabetes mellitus is Wolfram Syndrome, which arise from mutations in wolframin gene found on chromosome 4. Optic nerve atrophy, diabetes insipidus, sensorineuronal deafness, psychiatric problems can accompany diabetes mellitus.

Hypergonadotrophic hypogonadism can be rarely observed in Wolfram syndrome. A case of novel homozygous mutation in the wolframin gene has been reported because of concomittant rarely reported hypergonadotrophic hypogonadism.

### CASE PRESENTATION

#### INDEX CASE

- ✓ 3500 gr, term birth
- ✓ Parents are 2. degree cousins
- ✓ **Diabetes Mellitus:** When he was 2 years and 10 months old, attended with typical symptoms ( polyuria and polydipsia)  
Blood glucose: 234 mg/dl  
Hba1c: % 10
- ✓ **Diabetes insipidus:** Has not yet emerged
- ✓ **Optic atrophy:** Detected when he was 10 years old
- ✓ **Hearing loss:** Has not yet emerged
- ✓ **Psychiatric problems:** Has not yet emerged

The patients pubertal development was consistent with Tanner Stage 2 when he was 12 years and 10 months old. Testicular volumes rise up to 10 ml bilaterally and after all started to decrease.

- ✓ Initially: LH (luteinizing hormone): 20.9 mIU/ml, FSH ( follicular stimulating hormone): 49.9 mIU/ml and Total Testosteron: 347 ng/dl
- ✓ Spermogram revealed azoospermia
- ✓ Testosteron levels decreased gradually and Intramuscular testosteron replacement started

#### OLDER SISTER

- ✓ **Diabetes mellitus:** Diagnosed at 5 years old
- ✓ **Optic atrophy:** Detected when she was 9 years old
- ✓ **Diabetes insipidus:** Detected when she was 10 years old
- ✓ **Additionally:** Bladder dysfunction was present
- ✓ Patient died because of urosepsis when she was 27 years old.

Pubertal development: When she was 12 years old pubertal status was appropriate with Tanner stage 2.

- ✓ Spontaneous progression was observed.
- ✓ Menarch started at the age of fourteen. 9 months after menarch secondary amenorhea developed and hypergonadotrophic hypogonadism was observed.
- ✓ Hormone replacement treatment started after then.

### CONCLUSION

DIDMOAD syndrome should be considered in patients who are diagnosed with antibody negative diabetes mellitus. It is well known that diabetes insipidus and optic atrophy may develop in the follow-up of these patients, but it should be kept in mind that rarely hypergonadotrophic hypogonadism may also accompany Wolfram syndrome.

As in the presented case **hypergonadotrophic hypogonadism** can be a feature of reported mutation

GENETIC ANALYSES: c.2069G>A / p.(Cys690Tyr) homozygos mutation detected as likely pathogenic\*

\* The genetic examination was performed by University of Exeter Medical School

