

# A Boy with Wolfram Syndrome

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## INTRODUCTION

Wolfram syndrome, also known as DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, Deafness), is a rare neurodegenerative disease of autosomal recessive inheritance with incomplete penetrance. In addition, it may present with different endocrine and metabolic abnormalities such as pituitary dysfunction.



Bilateral optic atrophy with no retinopathy

## METHODS

We reported the clinical features, biochemical features and mutational analysis of a boy with Wolfram syndrome.

## RESULTS

A 7-year-old boy presented to ophthalmologist with bilateral blurred vision and found to have bilateral cataract. On further enquiry, the family noted 3-month history of polyuria, polydipsia and nocturia. There was no consanguinity and only paternal grandfather had type 2 diabetes at old age. Fasting glucose was 18 mmol/L. He had ketosis but no acidosis. HbA1c was 18.2% at presentation. Anti-islet cell antibody was negative. He received basal-bolus insulin at 0.8 unit/kg/day. He had undergone bilateral phacoemulsification of cataract and implant of intraocular lens soon after diagnosis. His vision remained clear after operation. His glycaemic control was also satisfactory with HbA1c ranged from 6.5% to 7.7%. He started to have onset of puberty at 9 years 8 months. However, he presented to ophthalmologist again at 11 years for drop in vision. Examination revealed bilateral pale optic disc rims with increased cup-to-disc ratio. Visual field examination demonstrated moderate field constriction. In view of diabetes mellitus and bilateral optic neuropathy, Wolfram syndrome was suspected. Mutational analysis detected a compound heterozygous c.1999C>T (Q667X) and c.2170C>T (P724S) mutations in WFS1 gene. Mutational analysis of parents confirmed their carrier status. He is now 18 years 2 months and he has achieved his final height comparable to mid-parental height. He so far did not develop diabetes insipidus, hearing impairment or neuropsychiatric manifestation.

## CONCLUSION

Although no clear genotype-phenotype correlation has been drawn for Wolfram syndrome, it is speculated that inactivation of both WFS1 alleles may be associated with an early onset of diabetes mellitus.

## REFERENCES

1. Aloi C, et al. Wolfram Syndrome: New Mutations, Different Phenotype. *PLoS ONE*. 2012;7(1):e29150.
2. Matsunaga K, et al. Wolfram Syndrome in the Japanese Population; Molecular Analysis of WFS1 Gene and Characterization of Clinical Features. *PLoS ONE*. 2014;9(9):e106906.
3. Chausseot A, et al. Mutation Update and Uncommon Phenotypes in a French Cohort of 96 Patients with WFS1-Related Disorders. *Clin Genet*. 2015;87(5):430-9.

