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X-linked Intellectual Disability Syndrome Associated with an *OGT* Gene Mutation: A Case Report

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Introduction

❖X-linked intellectual disability (XLID) accounts for approximately 5-10% of intellectual disability (ID) in males. Among these, *OGT* encodes O-GlcNAc transferase, essential for embryonic development and neural function, and pathogenic variants in the *OGT* gene cause XLID106.

❖We report a case of a male patient with XLID106 diagnosed through whole genome sequencing (WGS), describing his longitudinal developmental trajectory and rehabilitation management.

Case Report

❖A 6-month-old boy was referred to the department of rehabilitation medicine for developmental delay (DD). He was born at full-term following an uncomplicated pregnancy, with a birth weight of 3,850 g. The family pedigree is shown in Figure 1. Initial evaluation revealed gross motor delay at the 4-6 month level, including poor head control in the prone position and the ability to sit only with bilateral hand support, while other domains were age-appropriate. Dysmorphic features included long philtrum, broad nasal root, and large ears (Figure 2). Brain MRI showed no abnormalities.

❖The patient underwent rehabilitation therapy, and his developmental progress was monitored longitudinally. At 37 months of age, the Bayley Scales of Infant and Toddler Development III revealed global developmental delay (GDD) with cognitive, language, and motor composite scores below the 5th percentile (Table 1). Childhood Autism Rating Scale yielded a score of 30.5, suggesting mild-to-moderate autism spectrum features. Subsequent assessment revealed moderate ID (IQ 42). Chromosomal microarray analysis identified a 2.26 Mb duplication at 8p23.2 region, classified as a variant of uncertain significance and was not considered to fully explain the patient's presentation. Further genetic evaluation using WGS was performed, and revealed a hemizygous *OGT* variant, c.1358G>T (p.Arg453Leu).

❖Clinically, the patient exhibited features consistent with previously reported XLID106 cases: GDD, hypotonia, language impairment, autism spectrum traits, and ID. Previous reports of XLID106 have described associated features including short stature, cardiac anomalies, and hypothyroidism. However, routine laboratory studies and echocardiography revealed no abnormalities. Growth parameters remained within normal ranges throughout follow-up.

❖Sanger sequencing identified the same variant in a heterozygous state in the patient's mother and maternal half-sister. The maternal uncle, who had a history of DD and ID, was found to carry the variant in a hemizygous state, supporting its pathogenicity.

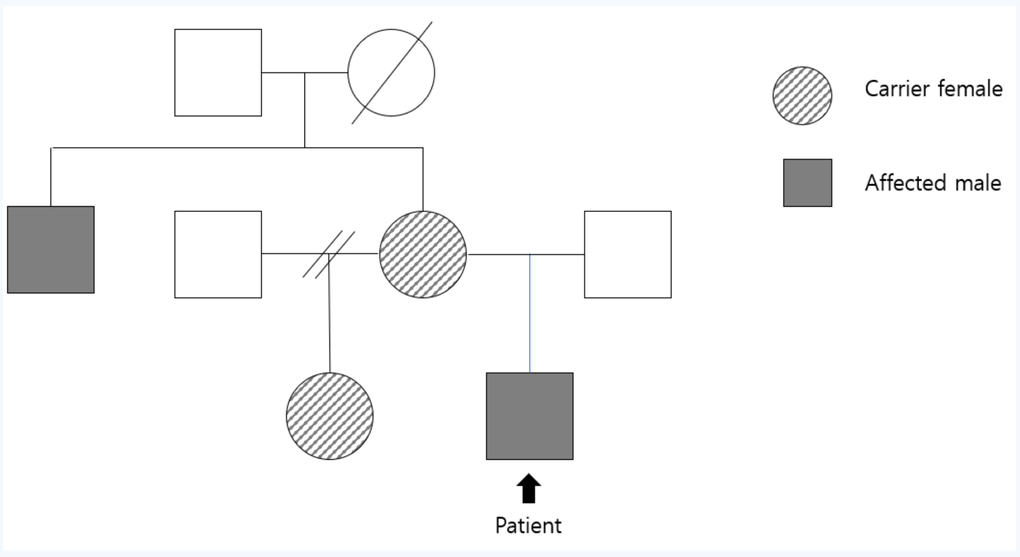

Figure 1. Pedigree of the family showing an X-linked inheritance pattern of the *OGT* variant. Squares indicate undetermined males; circles indicate undetermined females. Filled symbols represent affected individuals; symbols with diagonal lines indicate heterozygous carriers.

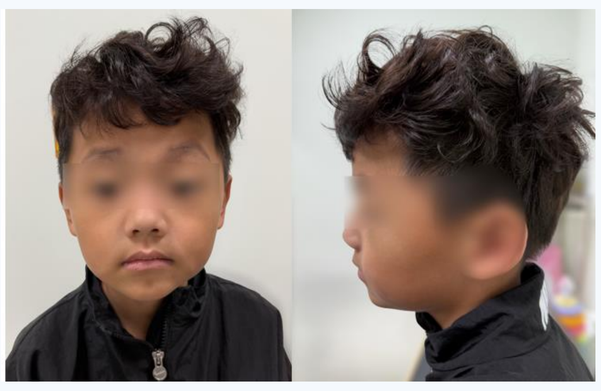

Figure 2 . Facial photographs of patient with *OGT* gene mutation.

Table 1. Results of DDST-II and BSID-III

DDST-II					
		At 7 mo	At 15 mo	At 50 mo	At 5 yr	At 6 yr
Personal-social		6-7	5-7	20-26	3~3.5	4-4.5
Fine motor-adaptive		6-8	9-11	24-36	3-3.5	4-4.5
Language		6-8	7-9	20-24	3-3.5	3.5-4
Gross motor		4-6	9-11	36-42	4-4.5	4-4.5
BSID-III						
					15 mo	**37 mo**
Cognitive	Scaled Score				1	4
	Composite Score				55	70
	Composite Percentile Rank				**0.1st**	**2nd**
Language	Scaled Score				9	10
	Composite Score				68	71
	Composite Percentile Rank				**2nd**	**3rd**
Motor	Scaled Score				11	9
	Composite Score				73	67
	Composite Percentile Rank				**4th**	**1st**
Social-emotional	Scaled Score				8	2
	Composite Score				90	60
	Composite Percentile Rank				**25th**	**0.4th**
Adaptive	Scaled Score				69	38
	Composite Score				75	56
	Composite Percentile Rank				**5th**	**0.2nd**

Values are presented as range or score. BSID-III, Bayley Scales of Infant and Toddler Development-3rd edition; DDST-II, Denver Developmental Screening Test-II.

Conclusion

❖We report a case of XLID106 caused by a hemizygous *OGT* variant c.1358G>T with familial segregation supporting pathogenicity. This case illustrates that early motor delay may precede GDD and ID in OGT-related XLID106, and that meaningful functional gains may be achievable with early intervention. Early intervention, including physical therapy, speech-language therapy, and behavioral therapy, is essential for optimizing developmental outcomes. Furthermore, family-based genetic counseling plays an important role in confirming inheritance patterns, facilitating early diagnosis, guiding individualized rehabilitation planning, and supporting affected families.