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AUTS2 gene mutation with 6q25.1 deletions : A Case Report

Kyung Hyun Park, M.D.[1*], Hye Jung Park, M.D., Ph.D.[1], Myungshin Kim, M.D., Ph.D.[2], Hoon Seok Kim, M.D., Ph.D.[2] , Joo Hyun Park, M.D., Ph.D.[1†]

[1] Department of Rehabilitation Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea

[2] Department of Clinical Laboratory Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea

Introduction

The AUTS2 gene influences neurodevelopment and is linked to various neurological disorders such as autism spectrum disorder, intellectual disability, developmental delay. Deletions in chromosome 6 long arm led to specific phenotypes, particularly in the intermediate region (6q15-q25) region, which includes developmental delay, hypotonia, postnatal growth retardation, congenital heart defects, and dysmorphic features. We present a case of a 4-year-old boy with developmental delay, hypotonia, and various congenital malformations with a mutation in the AUTS2 gene and a 0.12 Mb deletion at 6q25.1.

Case

The patient was born via cesarean section at 38 weeks of gestation. He was admitted to the neonatal intensive care unit for respiratory problems and at one month of age, he underwent repair of the diaphragmatic hernia. After discharge home, the patient was referred for evaluation and treatment of developmental delay and feeding difficulties at three months of age. The patient exhibits difficulty in controlling head with overall low trunk tone. Additionally, the patient presents with macrocephaly, a high arched palate, low set ears, and a simian crease, and triphalangeal thumbs. Brain magnetic resonance imaging (MRI) revealed cerebral atrophy in the frontal area. Karyotyping was normal. Next-generation sequencing (NGS) testing was performed for hereditary skeletal dysplasia disorders, and mutation of AUTS2 gene (c.1777A>G, heterozygous) was identified. However, upon conducting family testing, the same genetic mutation was observed in the patient's father, leading to the conclusion that it was not clinically significant. Patient returned clinic at the age of 3 for microarray testing. Global developmental delay was noted, with a social age of 0.47 years on social maturity testing and a severe autism score of 43.5 on the Korean version of the Childhood Autism Rating Scale. Microarray analysis revealed a 123Kb deletion at q25.1 of chromosome 6 in the patient. However, upon conducting family testing, the same variant in the unaffected older sibling, suggesting low clinical significance of the patient's abnormalities.

Conclusion

In this case patient's genetic tests (NGS and microarray) revealed mutations consistent with unaffected family members, suggesting no clinical significance. However, considering the developmental delay, hypotonia, and pre- and postnatal growth retardation observed in the patient with a 0.12Mb deletion at 6q25.1, along with the potential manifestations of mental retardation, autism, and cerebellar hypoplasia associated with AUTS2 gene mutations, it is not sufficient to simply conclude that there is no clinical significance. Rather, a comprehensive interpretation of the results is necessary, considering various factors, to determine clinical relevance. Furthermore, additional research is needed to investigate whether each mutation influences the others.

Developmental evaluation (The Bayley III)	Patient (8months of age)		Patient (40months of age)	
	DAE	Composite score	DAE	Composite score
Cognitive	3 months	55	5months	55
Receptive communication	2 months	65	4months	47
Expressive communication	3 months		9 months	
Fine motor	4 months	55	4 months	46
Gross motor	6 months		5 months	
Social-emotional	-	55		60
Adaptive behavior	-	46		41

DAE; Developmental age equivalent

Table 1. Developmental evaluation of the patient using the Bayley III scales of Infant Development

	Clinical features	NGS and microarray results	
		AUTS2 gene c.1777A>G	*6q25.1del 123Kb*
Patient's father	No specific features	Detected	Detected
Patient's mother	No specific features	Not Detected	*Unknown**
Patient's older brother	No specific features	Not Detected	Detected
The patient	Severe Developmental delay	Detected	Detected

**Related microarray evaluation was not performed*

Table 2. Findings of targeted next generation sequencing (NGS) and microarray in the patient's family. Identical AUTS2 gene mutation and 6q25.1del were detected in the family, even without clinical features

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number : HR22C160504)