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3q29 Microduplication Syndrome in Developmental Delay Children : A Case Report

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Introduction

Microduplications are chromosomal duplications that are too small to be detected by a conventional optical microscope. They are typically between 1 to 3 megabases in size and contain multiple genes. Some may be pathogenic, while others may be associated with disease susceptibility or resistance. Microduplications can also be inherited from normal parents, and sometimes identified in normal individuals. Interstitial duplications of 3q29 is a microduplication that is considered to be a new genetic syndrome with a neurodevelopmental phenotype. In this case report, we introduce siblings with a confirmed microduplication of the 3q29.

Case presentation

Two siblings born without any medical history at birth, both presented with developmental delay. Sibling A was born by cesarean section at 41 weeks of gestation weighing 3.5 kg and started walking at a chronological age of 16 months. The Korean Bayley Scales of Infant Development-III (K-BSID-III) performed at 42 months of age showed borderline results in gross motor, fine motor. In addition, developmental delay was shown in cognitive, receptive and expressive language at 25, 20 and 20 months level, respectively (Table 1). Chromosomal microarray (CMA) showed duplication of approximately 558 kilobases in the 3q29 region, with major Online Mendelian Inheritance in Man (OMIM) genes including SLC51A, PCYT1A, RNF168, WDR53, FBXO45, and NRROS. Sibling B was born by cesarean section at 37 weeks of gestation weighing 3.3 kg and started walking at chronological age of 14 months. K-BSID-III performed at 26 months showed below average results in gross motor, fine motor. Furthermore, developmental delay was shown in cognitive, receptive and expressive language at 17, 7, and 9 months level, respectively (Table 1). Brain magnetic resonance image (MRI) showed no abnormalities on both siblings (Figure 1). CMA showed duplication of approximately 556 kilobases in the 3q29 region, containing the same genes as sibling A.

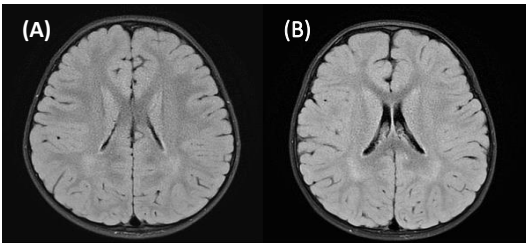

Figure 1. (A) Brain MRI of sibling A. (B) Brain MRI of sibling B.

Discussion

Nearly identical duplications were observed in both siblings. The phenotype of both siblings were similar with developmental delay in language and cognition compared to relatively intact gross and fine motor. No structural abnormalities of the brain were observed.

Interstitial duplications of 3q29 were previously thought to be probably benign. However, many recent case reports have shown pathogenic potential. In particular, recent studies have shown that the gene involved in this case, FBXO45, which encodes a protein-ubiquitin ligase, is known to play an important role in central and peripheral neural development. In addition, the length of the microduplications found in two siblings and the genes involved appear to be highly similar in this case report. The pathogenic potential of 3q29 microduplication syndrome requires further studies with other cases involving different genes.

		Korean Bayley Scales of Infant Development-III				
	Chronological Age at test	Cognition Index	Receptive & Expressive Language Index	Fine & Gross Motor Index	Social Emotion Index	Adaptive Behavior Index
A	42 months	65	58	73	90	76
B	26 months	60	46	82	75	61

Table 1. The result of K-BSID-III of siblings.