Human Genetics Asia 2023
68th Annual Meeting of the Japan Society of Human Genetics(JSHG)
P1-03-9
Tokyo, Japan Oct 11-14 2023

PGT-M of duplicated Duchenne muscular dystrophy suspected to be germline mosaicism

Ammae M, Nakano T, Yamauchi H, Nakaoka Y, Morimoto Y

Duplicated DMD, 10% of DMD cases, is typically diagnosed using the MLPA method when sample DNA like peripheral blood is available. However, in PGT-M genetic analysis using about 10 embryonic cells, MLPA is unusable, requiring a different direct method. We discuss a challenging PGT-M case for duplicated DMD, suspected germline mosaicism, where we used haplotype analysis, an indirect method, alongside the direct method.

The first and third children had an exon3-9 duplication identified via MLPA, but the mother's peripheral blood showed no duplicate variant, suggesting potential germline mosaicism. The couple, aiming for PGT-M, received approval from the Japan Society of Ob/Gy.

In the preliminary test for PGT-M, a diagnostic method for duplicated DMD was established using both an indirect method, leveraging the matched haplotypes of the first and third children, and a direct method that amplifies the DNA between the two duplicated exons using PCR.

The diagnosis of a single blastocyst in PGT-M was deemed indeterminable due to the inconsistency between the results of the direct method, which did not detect the duplicated variant, and the indirect method that had the same haplotype as the proband.

The indeterminate diagnosis was attributed to germline mosaicism. Possessing the same haplotype as the proband may still result in a non-affected wild-type embryo. A PGT-M diagnosis needs consistency between direct and indirect methods. Given the lack of definitive diagnostic tools for wild types in germline mosaicism, accurate diagnosis from a single embryo result was challenging.