

Microarray in clinical practice – utility vs complexity. Mixed phenotype of duplication 15q11.2q13.1 and deletion 16p11.2

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Introduction: There's a consensus to perform chromosomal microarray technique as first-tier clinical diagnostic test for individuals with developmental disabilities. However, given the complexity of clinical presentations, often several diagnostic methods are held before conducting microarray.

Method: We report the case of a 5 year-old boy referred to Medical Genetics due to short stature, developmental disabilities and facial dysmorphic features.

He was born from eutocic delivery after an uneventful pregnancy. He had psychomotor milestones delayed like sitting at 9 months and walking at 24 months, holding an immature broad-based gait. There was history of learning difficulties from both parents, and the mother has also short stature.

On examination it was noted some facial dysmorphic features like high forehead, conical canines and rarefaction of the distal portion of the eyebrows.

Due to the history of an episode of transient ataxia, and suspicion of an inherited metabolic disorder, he had already performed various analytical and imaging screenings, all normal.

Results: Chromosomal microarray analysis revealed two pathogenic Copy Number Variants (CNV's): 16p11.2 deletion and 15q11.2q13.1 duplication.

The 15q11q13 microduplication syndrome (OMIM # 608636) is a very rare clinical entity with about 30 reported cases with maternal origin, and it is characterized by neurobehavioral disorder, hypotonia, cognitive impairment, epilepsy and short stature.

The 16p11.2 microdeletion syndrome (OMIM # 613444) is also a rare clinical entity, with high penetrance, associated with obesity and developmental disabilities.

Discussion: Despite the unquestionable utility of microarray, the correlation of the CNV's with the phenotype is often difficult by the rarity of these new microdeletion/duplication clinical entities. In this case the interpretation has increased difficulty because of the simultaneous existence of two distinct clinical entities. Segregation studies, which in the first step include parental analysis, are essential for genetic counseling and determining the risk of recurrence but also for a more accurate correlation genotype-phenotype.