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My46 Trait Profile

1q21.1 microdeletion

1q21.1 microdeletion results from a loss of genetic material on one of the long arms of chromosome 1. This deletion results in the loss of several genes.

Characteristics of 1q21.1 microdeletion

1q21.1 microdeletion is quite variable depending on the size of the deletion as well as other genetic and environmental factors. Some individuals have no obvious birth defects with normal developmental progress and subsequently normal intelligence. However individuals with 1q21.1 microdeletion have an increased risk for developmental delays (typically mild), neuropsychological concerns such as ADHD and autism, microcephaly (smaller than expected head size), cataracts (clouding of the lens of the eye), and certain birth defects (most commonly heart defects).

Some individuals with very specific deletions involving a gene known as RBM8A may be at risk for a syndrome known as TAR (thrombocytopenia-absent radius) syndrome. TAR syndrome can have additional features including the absence or abnormality of a bone in the forearm known as the radius, a deficiency of platelets (thrombocytopenia) which can inhibit normal blood clotting, intolerance to cow's milk, and other skeletal problems.

Diagnosis/Testing

This condition is caused by a deletion (missing piece) of genetic material on one of the two copies of chromosome 1 in each cell. A microarray (also known as an oligoarray, SNP array or arrayCGH) is a blood test which can simultaneously evaluate the cells for small pieces of genetic material that may be missing or extra on each chromosome (the packages of genetic material). A blood test known as FISH (fluorescence in situ hybridization) involves attaching fluorescent probes to the specific area of interest and is frequently used for testing family members of affected individuals.

At least three specific genes within this region have been linked to some of the key features observed for individuals with 1q21.1 microdeletion. The GJA5 gene has been associated with causing isolated congenital heart defects, the RBM8A has been associated with causing the features observed in TAR syndrome and the GJA8 gene has been associated with causing eye abnormalities such as cataracts.

Management/Surveillance

Development assessments, as well as evaluations of the heart and eyes are suggested at the time of diagnosis if not already performed. Other monitoring may be necessary given each child's unique symptoms.

Mode of inheritance

1q21.1 microdeletion is inherited in an autosomal dominant pattern. This means inheriting one 1q21.1 microdeletion is usually enough for an individual to be affected and show signs of 1q21.1 microdeletion. The deletion can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Risk to family members

The risk to family members depends on whether or not the individual with 1q21.1 microdeletion has a parent with

the deletion. If a parent also has the deletion, the risk for that parent to have another child with the deletion is 50% with each pregnancy. If a parent does not have the deletion, the risk of other siblings being affected is very low.

Special considerations

For those individuals with features of TAR syndrome or a deletion specifically involving the RBM8A gene, a CBC (complete blood count) with platelets may be considered as well as specific genetic testing to determine whether the other copy of the RBM8A gene is “spelled” correctly. Some individuals with symptoms of TAR syndrome are missing one copy of this particular gene and have a mutation or misspelling in the other copy.

Resources

Genetics Home Reference: 1q21.1 microdeletion
http://ghr.nlm.nih.gov/condition/1q211-microdeletion
Simons VIP Connect Registry
http://www.simonsvipconnect.org/forms/FactSheet1qDeletion.pdf
Unique: Understanding Chromosome Disorders
http://www.rarechromo.org/information/Chromosome%20%201/1q21.1%20microdeletions%20FTNW.pdf

References

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Mefford, HC. et al. (2008)."Recurrent rearrangements of chromosome 1q21.1 and variable pediatric phenotypes." New England Journal of Medicine 359(16): 1685-1699.
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