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ABOUT US

Chromosome Disorder Outreach provides support and information to anyone diagnosed with a rare chromosome change, rearrangement or disorder. CDO actively promotes research and a positive community understanding of all chromosome disorders.

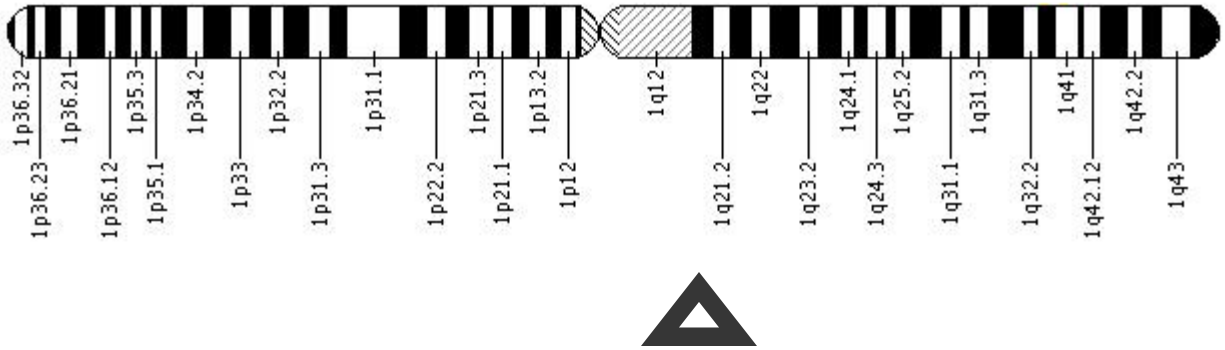
CDO is a 501c3 organization founded in 1992.

1q21.1 Deletion Syndrome

Deletion 1q21.1

The genetic size of the whole chromosome 1 is ~246 Mb. The segment 1q21.1 occupies only ~4 Mb (from ~141.5 Mb to 145.9 Mb) and both deletions and duplications within this segment became recognizable only for the last years when molecular cytogenetic methods became available.

There are two conditions, related to deletions 1q21.1. There is a well-know syndrome TAR (Thrombocytopenia – Absent Radius). The main manifestations of this entity are evident from its title. Thrombocytopenia may be accompanied by leucopenia. The characteristic defect of extremities is an absence of radial bones with preservation of thumbs (in most other syndromes when radial bones are absent the thumbs are absent also). TAR was considered to be an autosomal-recessive condition.



The molecular studies showed a very small deletion 1q21.1 [only ~350 Kb (from 144.1 Mb to 144.5 Mb)] in all persons with this syndrome. This segment contains more than 10 genes, but it remains unclear, which of these genes contributes for the occurrence of TAR syndrome. Although in most patients this deletion occurred de novo, in ~25% of families the same deletion was found in one of the healthy parents. Therefore deletion is necessary but not sufficient for the occurrence of TAR-syndrome. Further examinations showed that all patients with deletion 1q21.1 and TAR syndrome reveal that above this deletion they have an “innocent” variant of non-coding DNA, inherited from another parent (1). This variant does not cause any problem, but its interaction with deletion leads to serious defects. Mechanisms of this interaction remain not very clear.

The other condition, related to 1q21.1 deletion is caused by much larger deletion of the more distal part of 1q21.1 (144.8 Mb -145.9 Mb). Sometimes to distinguish from “proximal” or “TAR-related” 1q21.1 deletion this deletion is called the “distal 1q21.1 deletion”. Frequent occurrence of deletions (and symmetrical duplications) in this area is caused by the genetic structure of this region, allowing non-allelic homologous recombination.

At first this deletion was found in several patients with congenital heart disease. Later it became evident that manifestations of this condition are very variable. Currently it is very difficult to present a real clinical spectrum of this deletion because different groups had different criteria of selection of the patients for chromosomal examination.

Facial features in most patients include frontal bossing, deep set eyes and bulbous nose (2,3), although this condition is unrecognizable upon only clinical examination.

Congenital heart disease is found more than in 25% of patients (4). Although most of heart defects are relatively mild (bicuspid aortic valve, septal defects, patent ductus arteriosus) some patients have very serious defects (interrupted aortic arch, arterial trunk, transposition of great arteries).

Different types of polydactyly were found in 10%-15% of patients. Trigonocephaly, hydrocephaly, cleft palate, microphthalmia, cataracts were also repeatedly reported. There are isolated descriptions of numerous other defects such as absence of one kidney, hydronephrosis, pyloric stenosis etc. However, at least half patients with this deletion do not have any birth defects (above some peculiar facial features, if any). The patients may suffer from seizures (2,5). There are indications that this deletion may be associated with autism and schizophrenia although sometimes the presence of autism and/or schizophrenia was a criterion for selection of patients for study.

It is obvious that a real clinical picture of the “distal” 1q21.1 deletion will become clear when it will be possible a) to implement a common protocol for evaluation and description of these patients; b) to follow up the children who were too young at the moment of the examination.

The size of deletion may vary, but typically it is between 1.0 and 1.9 Mb. In some persons deletion involves also TAR-region but it does not cause any additional abnormalities (deletion of TAR-region may produce abnormal findings only which accompanied by other genetic factors).

Most 1q21.1 deletions occurs de novo. However, in many families the same deletion may be found in one parent (mother or father) who manifest some mild manifestations [minimal dysmorphism, learning disability or psychological problems] or are clinically normal. The normal phenotype in persons with microdeletions may suggest that some microdeletions (including, but not limited to del 1q21.1) may require some additional genetic variants to produce clinical manifestations (6). Unmasking of some mutated genes is another explanation for the occurrence of abnormal findings.

Genetic prognosis will depend on the karyotype of the parents. The recurrence risk is negligible if the parental chromosomes are normal. If one parent has asymptomatic deletion the chance to inherit this deletion will be 50% but its clinical significance remains uncertain.