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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.

9q34.3
KLEEFSTRA SYNDROME

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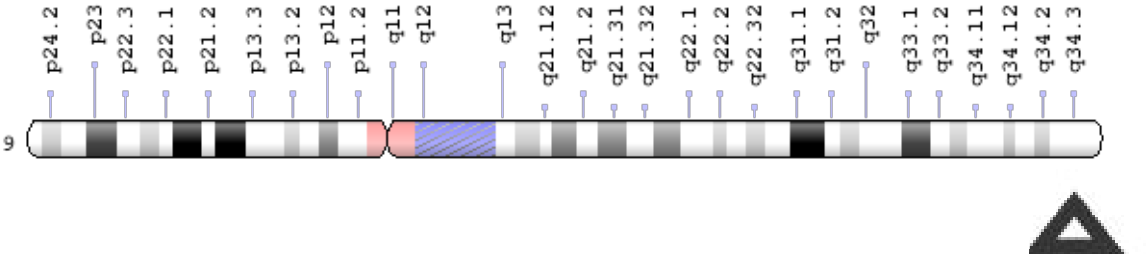
Kleefstra syndrome (KS) is a rare genetic disorder usually caused by a deletion of thesubtelomeric part of chromosome 9 (9q34.3). It was delineated in the 2000's when telomeric FISH probes and – later – molecular cytogenetic tests became a common practice of cytogenetic examinations. The most accurate description of the condition was provided by a Dutch geneticist Tjitske Kleefstra and her team[1], and the term KS has now actually replaced the old name "9q subtelomeric deletion syndrome".The incidence of KS is now known. There are at least 120 reported cases of this condition and many more patients are being reported each year.



The main manifestations of KS are intellectual disability, hypotonia in childhood and dysmorphic features. The latter are relatively mild, and the possibility of recognition of KS before genetic examination seems doubtful.

Developmental disability is a constant finding, although the degree of disability varies from one patient to another. Generally, disability is serious: most patients can speak only single words. As a rule they cannot read or write. Hypotonia (low muscle tonus) is typical for small babies with KS, but usually disappears in older children.

Dysmorphic features include synophrys, hypoplastic middle part of the face, everted lower lip, protruding tongue. The upper lip is sometimes described as "cupid". It should be noted, however, that similar features may be found in many other forms of chromosomal disorders. Approximately half of patients are microcephalic, but severe microcephaly is not typical. In many patients microcephaly may be associated with brachycephaly.

Congenital heart defects are found in at least 40% of patients2, but in most cases these defects are relatively mild and do not require surgical treatment. Gastro-esophageal reflux is common, but structural defects of the gastro-intestinal system are very rare (there are several reports of anal atresia). Defects of the kidneys are represented mainly by vesico-urinary reflux. At least one third of KS patients are overweight.

Epilepsy occurs in ~35% of patients. Regression in cognitive abilities has been noted in several persons. Behavioral problems are mentioned in half of the patients. They include attention deficit disorder, autistic features, apathy, self-mutilation, sleep disturbances and emotional outbursts.

The size of deletions varies from case to case, and not a single breakpoint seems to be typical. Although deletions involve several genes the loss of the EHMT1 gene is sufficient to produce the full phenotype of KS. Deletions of neighboring genes do not lead to additional clinical abnormalities. At the same time isolated deletions of neighboring genes (not involving EHMT1 gene) do not produce the phenotype of KS.

It has been shown that point mutations in the EHMT1 gene lead basically to the same complex of abnormalities as deletions of this gene. That is why the term KS is currently used both for conditions involving deletions of the EHMT1 gene and for conditions where this gene is mutated[2,3].

In almost all instances KS is a result of a sporadic deletion (or mutation). In very rare cases one of the parents may be found to be an asymptomatic carrier of the deletion at least in part of the cells.