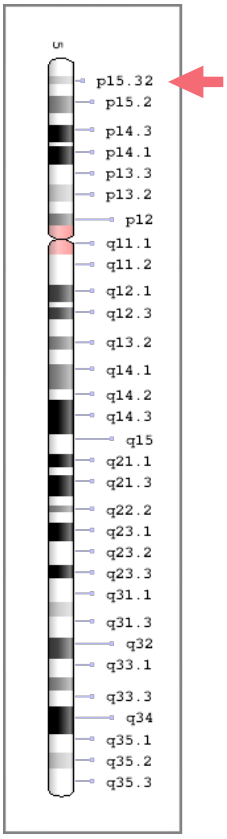
DELETION 5P13.2

Deletion 5p13.2 and Cornelia de Lange Syndrome



Cornelia de Lange syndrome (CdLS) is a well-known disorder. In typical cases this condition is characterized by severe prenatal hypoplasia (and postnatal growth delay), microcephaly, facial dysmorphism and multiple abnormalities of the extremities. The most common internal defects are diaphragmatic hernia and intestinal malrotation. Dysmorphic features include long eyelashes, thick eyebrows, synophrys (a single long eyebrow over the eyes and bridge of the nose), thin upper lip vermillion, and anteverted nares. Additionally, many patients have hirsutism. Besides micromelia (shortness of the extremities), most patients have ectrodactyly, oligodactyly, or even monodactyly of the upper extremities. Many fetuses with CdLS do not survive till birth. Children with this syndrome reveal significant developmental delay, autism and self-injurious behavior[1].

The syndrome is relatively common, as it is found in approximately 1:10,000 to 1:30,000 live births. Virtually all cases of the CdLS are sporadic and there is no recurrence in the families. Although this syndrome has been reported for more than 90 years, its origin was basically unknown till the 2000's. Recently, it was shown that most cases of the CdLS are caused by defects of the NIPBL gene, located at the short arm of chromosome 5 (5p13). It should be mentioned that CdLS is a genetically heterogeneous condition and at least 1/3 of cases are caused by defects in other known genes (or by

unknown reasons). However, haploinsufficiency of the NIPBL gene is the main cause of the syndrome, and defects of this gene are found in almost all “typical” cases.

NIPBL functions as a cohesion whose job is to help regulate the holding together of sister chromatids during cell division. Additionally, NIPBL functions to regulate the expression of other genes[2].

In most patients CdLS is caused by mutations within the NIPBL gene, but there are several dozen reports when this syndrome was caused by deletions of 5p13 involving this gene. It’s interesting that deletion of the segment 5p13-pter was mentioned in a patient with a typical CdLS phenotype in 1981[3], although the authors did not recognize this syndrome in their case. Currently there are no differences between mutation- and deletion-caused patients with CdLS, although the accurate comparison is difficult due to relative rarity of deletion-caused cases.

Although a diagnosis of the typical cases of CdLS can be made prenatally based on abnormal ultrasound screenings, the disorder usually is diagnosed only postnatally[4].

Traditionally, deletions of the short arm of chromosome 5 are associated with cri-du-chat syndrome. However, cri-du-chat syndrome is caused by deletion of the most distal segments of 5p (5p14-5p15) and deletions of the 5p13 segment cause another genetic condition completely.

REFERENCES

[1]Kaur M, Blair J, Devkota B, et al. (2023). Genomic analyses in Cornelia de Lange Syndrome and related diagnoses: Novel candidate genes, genotype–phenotype correlations and common mechanisms. *Amer J Med Genet* v. 191, 2113-2131.

[2]Gervasini C, Parenti I, Picinelli C, et al. (2013). Molecular characterization of a mosaic NIPBL deletion in a Cornelia de Lange patient with severe phenotype. *Eur J Med Genet* v. 56, 138–143.

[3]Taylor MJ & Josifek K (1981). Multiple congenital anomalies, thymic dysplasia, severe congenital heart disease, and oligodactyly with a deletion of the short arm of chromosome 5. *Amer J Med Genet* v. 9, 5-11.

[4]Hulinsky R, Byrne JL, Lowichik A & Viskochil DH (2005). Fetus with interstitial del(5)(p13.1p14.2) diagnosed postnatally with Cornelia de Lange syndrome. *Amer J Med Genet* v. *137A*, 336–338.