5q31.3 microdeletion syndrome

Description

5q31.3 microdeletion syndrome is a condition characterized by severely delayed development of speech and motor skills, such as walking. Beginning in infancy, affected individuals also have weak muscle tone (hypotonia), feeding difficulties, and breathing problems. Breathing problems and difficulty swallowing (dysphagia) can be life-threatening.

5q31.3 microdeletion syndrome is also characterized by distinctive facial features. Such features include a narrow forehead, widely spaced eyes (hypertelorism), an open mouth with an upper lip that points outward (called a tented lip), a high arch in the roof of the mouth (high-arched palate), a small lower jaw (micrognathia), and a lack of facial expression. Some of these features, such as an open mouth with a tented lip and an expressionless face, are thought to be due to hypotonia.

Recurrent seizures (epilepsy) and seizure-like episodes (which can include muscle jerking, twitching, and stiffening), are common in 5q31.3 microdeletion syndrome. Many individuals with 5q31.3 microdeletion syndrome have brain abnormalities, several of which are caused by reduced production of myelin or delayed maturation of myelin. Myelin is the protective covering that insulates nerves and ensures the rapid transmission of nerve impulses.

Frequency

5q31.3 microdeletion syndrome is a very rare disorder. At least eight individuals with the condition have been described in the medical literature.

Causes

5q31.3 microdeletion syndrome is caused by a chromosomal change in which a small piece of chromosome 5 is deleted in each cell. The deletion occurs on the long (q) arm of the chromosome at a position designated q31.3. The size of the deletion can range from several thousand to several million DNA building blocks (base pairs). The deleted region typically contains at least three genes. The loss of one of these genes, *PURA*, is thought to lead to most of the characteristic features of the condition.

The protein produced from the *PURA* gene, called Pur-alpha (Purα), has multiple roles in cells, including controlling the activity of genes (gene transcription) and aiding in the

copying (replication) of DNA. This protein is especially important for normal brain development; it helps direct the growth and division of nerve cells (neurons) and may be involved in the formation or maturation of myelin.

A loss of one copy of the *PURA* gene is thought to alter normal brain development and impair the function of neurons, leading to developmental delay, hypotonia, seizures, and other neurological problems in people with 5q31.3 microdeletion syndrome. Some studies suggest that loss of another nearby gene increases the severity of the signs and symptoms. It is unclear how the loss of other genes in the deleted region contributes to the development of 5q31.3 microdeletion syndrome.

Learn more about the gene and chromosome associated with 5q31.3 microdeletion syndrome

- PURA
- chromosome 5

Additional Information from NCBI Gene:

- NRG2

Inheritance

5q31.3 microdeletion syndrome follows an autosomal dominant inheritance pattern, which means one copy of the genetic alteration in each cell is sufficient to cause the disorder.

The condition is not inherited but results from the deletion of a chromosomal segment during the formation of reproductive cells (eggs and sperm) or in early fetal development. Affected people typically have no history of the disorder in their family.

Other Names for This Condition

- Severe neonatal hypotonia-seizures-encephalopathy syndrome due to 5q31.3 microdeletion

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: PURA-related severe neonatal hypotonia-seizures-encephalopathy syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4015357/)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%285q31.3+microdeletion+syndrome%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Bonaglia MC, Zanotta N, Giorda R, D'Angelo G, Zucca C. Long-term follow-up ofa patient with 5q31.3 microdeletion syndrome and the smallest de novo 5q31.2q31.3deletion involving PURA. Mol Cytogenet. 2015 Nov 14;8:89. doi:10.1186/s13039-015-0193-9. eCollection 2015. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26582469) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4650292/)
- Brown N, Burgess T, Forbes R, McGillivray G, Kornberg A, Mandelstam S, StarkZ. 5q31.3 Microdeletion syndrome: clinical and molecular characterization of twofurther cases. Am J Med Genet A. 2013 Oct;161A(10):2604-8. doi:10.1002/ajmg.a.36108. Epub 2013 Aug 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23950017)
- Hosoki K, Ohta T, Natsume J, Imai S, Okumura A, Matsui T, Harada N, Bacino CA, Scaglia F, Jones JY, Niikawa N, Saitoh S. Clinical phenotype and candidate genesfor the 5q31.3 microdeletion syndrome. Am J Med Genet A. 2012 Aug;158A(8):1891-6.doi: 10.1002/ajmg.a.35439. Epub 2012 Jun 18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22711443)
- Shimojima K, Isidor B, Le Caignec C, Kondo A, Sakata S, Ohno K, Yamamoto T. Anew microdeletion syndrome of 5q31.3 characterized by severe developmentaldelays, distinctive facial features, and delayed myelination. Am J Med Genet A.2011 Apr;155A(4):732-6. doi: 10.1002/ajmg.a.33891. Epub 2011 Mar 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21594995)
- White MK, Johnson EM, Khalili K. Multiple roles for Puralpha in cellular andviral regulation. Cell Cycle. 2009 Feb 1;8(3):1-7. doi: 10.4161/cc.8.3.7585. Epub2009 Feb 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19182532) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2683411/)

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