PURA Syndrome

Subjects: Genetics & Heredity
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PURA syndrome is a condition characterized by intellectual disability and delayed development of speech and motor skills, such as walking.

genetic conditions

1. Introduction

Expressive language skills (vocabulary and the production of speech) are generally more severely affected than receptive language skills (the ability to understand speech), and most affected individuals are unable to speak. People with *PURA* syndrome may learn to walk later than their peers; many are never able to walk. In infancy, affected infants have very weak muscle tone (hypotonia) and feeding difficulties. Problems with swallowing (dysphagia) can last throughout life. In addition, affected infants can be excessively sleepy (hypersomnolent), have a low body temperature (hypothermia), and have short pauses in breathing (apnea) or episodes of abnormally slow breathing (hypoventilation). These breathing problems usually go away after age 1.

Recurrent seizures (epilepsy) are also common in *PURA* syndrome. Seizures usually begin before age 5 with uncontrolled muscle jerks (myoclonus). Other types of seizures can develop, such as generalized tonic-clonic seizures, which involve loss of consciousness, muscle rigidity, and convulsions. In people with *PURA* syndrome, seizures are often difficult to control.

Other features in people with *PURA* syndrome can include abnormalities of the heart, eyes, urogenital tract, gastrointestinal tract, and skeleton. Some affected individuals have symptoms of a hormonal problem, such as early sexual development (precocious puberty) or low levels of vitamin D (which is a hormone).

2. Frequency

PURA syndrome is a rare condition affecting at least 70 individuals. It is estimated to account for fewer than 1 percent of cases of developmental delay.

3. Causes

PURA syndrome is caused by mutations in the *PURA* gene, which provides instructions for making a protein called Pur-alpha (Purα). This protein has multiple roles in cells, including controlling the activity of genes (gene

transcription) and aiding in the copying (replication) of DNA. The Purα protein is especially important for normal brain development. Purα helps direct the growth and division of nerve cells (neurons). It may also be involved in the formation or maturation of myelin, the protective substance that covers nerves and promotes the efficient transmission of nerve impulses.

Mutations in the *PURA* gene are thought to lead to a reduced amount of functional Purα protein. Although it is not understood how a partial loss of Purα function leads to the signs and symptoms of *PURA* syndrome, researchers suspect that it may alter normal brain development and impair the function of neurons, leading to developmental problems and seizures in people with the condition.

The Gene Associated with PURA Syndrome

- PURA

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- PURA-related neurodevelopmental disorder
- PURA-related severe neonatal hypotonia-seizures-encephalopathy syndrome

References

1. Hunt D, Leventer RJ, Simons C, Taft R, Swoboda KJ, Gawne-Cain M; DDD study,Magee AC, Turnpenny PD, Baralle D. Whole exome sequencing in family trios revealsde novo mutations in PURA as a cause of severe neurodevelopmental delay andlearning disability. J Med Genet. 2014 Dec;51(12):806-13. doi:10.1136/jmedgenet-2014-102798.
2. Lalani SR, Zhang J, Schaaf CP, Brown CW, Magoulas P, Tsai AC, El-Gharbawy A,Wierenga KJ, Bartholomew D, Fong CT, Barbaro-Dieber T, Kukolich MK, Burrage LC,Austin E, Keller K, Pastore M, Fernandez F, Lotze T, Wilfong A, Purcarin G, ZhuW, Craigen WJ, McGuire M, Jain M, Cooney E, Azamian M, Bainbridge MN, Muzny DM,Boerwinkle E, Person RE, Niu Z, Eng CM, Lupski JR, Gibbs RA, Beaudet AL, Yang Y, Wang MC, Xia F. Mutations in PURA cause profound neonatal

hypotonia, seizures,and encephalopathy in 5q31.3 microdeletion syndrome. Am J Hum Genet. 2014 Nov6;95(5):579-83. doi: 10.1016/j.ajhg.2014.09.014.

3. Reijnders MRF, Janowski R, Alvi M, Self JE, van Essen TJ, Vreeburg M, RouhlRPW, Stevens SJC, Stegmann APA, Schieving J, Pfundt R, van Dijk K, Smeets E,Stumpel CTRM, Bok LA, Cobben JM, Engelen M, Mansour S, Whiteford M, Chandler KE, Douzgou S, Cooper NS, Tan EC, Foo R, Lai AHM, Rankin J, Green A, Lönnqvist T,Isohanni P, Williams S, Ruhoy I, Carvalho KS, Dowling JJ, Lev DL, Sterbova K,Lassuthova P, Neupauerová J, Waugh JL, Keros S, Clayton-Smith J, Smithson SF,Brunner HG, van Hoeckel C, Anderson M, Clowes VE, Siu VM, Ddd Study T, Selber P, Leventer RJ, Nellaker C, Niessing D, Hunt D, Baralle D. PURA syndrome: clinicaldelineation and genotype-phenotype study in 32 individuals with review ofpublished literature. J Med Genet. 2018 Feb;55(2):104-113. doi:10.1136/jmedgenet-2017-104946.
4. Reijnders MRF, Leventer RJ, Lee BH, Baralle D, Selber P, Paciorkowski AR, HuntD. PURA-Related Neurodevelopmental Disorders. 2017 Apr 27. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Availablefrom http://www.ncbi.nlm.nih.gov/books/NBK426063/
5. Tanaka AJ, Bai R, Cho MT, Anyane-Yeboa K, Ahimaz P, Wilson AL, Kendall F, Hay B, Moss T, Nardini M, Bauer M, Retterer K, Juusola J, Chung WK. De novo mutationsin PURA are associated with hypotonia and developmental delay. Cold Spring HarbMol Case Stud. 2015 Oct;1(1):a000356. doi: 10.1101/mcs.a000356.
6. White MK, Johnson EM, Khalili K. Multiple roles for Puralpha in cellular andviral regulation. Cell Cycle. 2009 Feb 1;8(3):1-7.