ADNP syndrome

ADNP syndrome is a condition that causes a wide variety of signs and symptoms. Its hallmark features are intellectual disability and autism spectrum disorder, which is characterized by impaired communication and social interaction. Affected individuals also have distinctive facial features and abnormalities of multiple body systems.

Individuals with ADNP syndrome have mild to severe intellectual disability and delayed development of speech and motor skills such as sitting and walking. Some affected individuals are never able to speak. People with this disorder exhibit features typical of autism spectrum disorder, including repetitive behaviors and difficulty with social interactions. ADNP syndrome is also associated with mood disorders or behavioral problems, such as anxiety, temper tantrums, attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder, or sleep problems.

Many people with ADNP syndrome have distinctive facial features, which most commonly include a prominent forehead, a high hairline, outside corners of the eyes that point upward or downward (upslanting or downslanting palpebral fissures), droopy eyelids (ptosis), a broad nasal bridge, and a thin upper lip. These individuals may also have unusually shaped ears or hand and finger abnormalities. Eye and vision abnormalities, such as eyes that do not point in the same direction (strabismus) and farsightedness (hyperopia), also occur in ADNP syndrome. Some people with this condition have early appearance (eruption) of primary (baby) teeth.

Some people with ADNP syndrome have weak muscle tone (hypotonia) and feeding difficulties in infancy. They may also have digestive system problems, such as backflow of stomach acids into the esophagus (gastroesophageal reflux), vomiting, and constipation. Other features that occur in ADNP syndrome include obesity, seizures, and heart abnormalities.

Frequency

The prevalence of ADNP syndrome is unknown. It is estimated to account for 0.17 percent of all cases of autism spectrum disorder, making it one of the most common genetic causes of this condition.

Causes

ADNP syndrome is caused by mutations in the ADNP gene. The protein produced from this gene helps control the activity (expression) of other genes through a process called chromatin remodeling. Chromatin is the network of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression
is regulated during development; when DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

By regulating gene expression, the ADNP protein is involved in many aspects of growth and development. It is particularly important for regulation of genes involved in normal brain development, and it likely controls the activity of genes that direct the development and function of other body systems.

Although it is unclear how mutations in the ADNP gene affect ADNP protein function, researchers suggest that the mutations result in abnormal chromatin remodeling. Disturbance of this process alters the activity of many genes and disrupts development or function of several of the body's tissues and organs, including the brain. These changes likely explain the intellectual disability, autism spectrum disorder, and other diverse signs and symptoms of ADNP syndrome.

Inheritance Pattern

ADNP syndrome is not inherited. It results from new (de novo) mutations in the ADNP gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. The condition occurs in people with no history of the disorder in their family.

Other Names for This Condition

- ADNP-related intellectual disability and autism spectrum disorder
- ADNP-related multiple congenital anomalies-intellectual disability-autism spectrum disorder
- Helsmoortel-van der Aa syndrome
- HVDAS
- mental retardation, autosomal dominant 28
- MRD28

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22ADNP+syndrome%22+OR+%22ADNP-related+intellectual+disability+and+autism+spectrum+disorder%22
Other Diagnosis and Management Resources

• GeneReview: ADNP-Related Intellectual Disability and Autism Spectrum Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK355518

Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Autism Spectrum Disorder
  https://medlineplus.gov/ency/article/001526.htm

• Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm

• Health Topic: Autism Spectrum Disorder
  https://medlineplus.gov/autism_spectrum_disorder.html

• Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmental_disabilities.html

Genetic and Rare Diseases Information Center

• ADNP syndrome

Additional NIH Resources

• National Institute of Neurologic Disorders and Stroke: Autism Spectrum Disorder Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Autism-Spectrum-Disorder-Information-Page

Educational Resources

• Centers For Disease Control and Prevention: Facts About Intellectual Disability

• MalaCards: adnp syndrome
  https://www.malacards.org/card/adnp_syndrome

• Merck Manual Consumer Version: Intellectual Disability

• Orphanet: ADNP syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=404448

• Simons Searchlight
  https://www.simonssearchlight.org/research/what-we-study/adnp/
• Undiagnosed Diseases Network: Participant Page
  https://undiagnosed.hms.harvard.edu/participants/participant-051/

• Unique: Rare Chromosome Disorder Support Group (UK)

Patient Support and Advocacy Resources

• ADNP Kids
  https://www.adnpkids.com/

• American Association on Intellectual and Developmental Disabilities (AAIDD)
  https://www.aaidd.org/

• Autism Society
  https://www.autism-society.org/

• Autism Speaks
  https://www.autismspeaks.org/

Clinical Information from GeneReviews

• ADNP-Related Intellectual Disability and Autism Spectrum Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK355518

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ADNP+syndrome%5BTIAB%5D%29+OR+%28Helsmoortel-van+der+Aa+syndrome%5BTIAB%5D%29%29+OR+%28%28ADNP%5BTIAB%5D%29+AND+%28autism%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• HELSMOORTEL-VAN DER AA SYNDROME
  http://omim.org/entry/615873

Medical Genetics Database from MedGen

• Helsmoortel-Van der Aa Syndrome
Sources for This Summary


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