Norrie disease

Norrie disease is an inherited eye disorder that leads to blindness in male infants at birth or soon after birth. It causes abnormal development of the retina, the layer of sensory cells that detect light and color, with masses of immature retinal cells accumulating at the back of the eye. As a result, the pupils appear white when light is shone on them, a sign called leukocoria. The irises (colored portions of the eyes) or the entire eyeballs may shrink and deteriorate during the first months of life, and cataracts (cloudiness in the lens of the eye) may eventually develop.

About one third of individuals with Norrie disease develop progressive hearing loss, and more than half experience developmental delays in motor skills such as sitting up and walking. Other problems may include mild to moderate intellectual disability, often with psychosis, and abnormalities that can affect circulation, breathing, digestion, excretion, or reproduction.

Frequency

Norrie disease is a rare disorder; its exact incidence is unknown. It is not associated with any specific racial or ethnic group.

Genetic Changes

Mutations in the *NDP* gene cause Norrie disease.

The *NDP* gene provides instructions for making a protein called norrin. Norrin participates in the Wnt cascade, a sequence of steps that affect the way cells and tissues develop. In particular, norrin seems to play a critical role in the specialization of retinal cells for their unique sensory capabilities. It is also involved in the establishment of a blood supply to tissues of the retina and the inner ear, and the development of other body systems.

In order to initiate the Wnt cascade, norrin must bind (attach) to another protein called frizzled-4. Mutations in the norrin protein interfere with its ability to bind to frizzled-4, resulting in the signs and symptoms of Norrie disease.

Inheritance Pattern

This condition is inherited in an X-linked recessive pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation must be present in both copies of the gene to cause the disorder. Males are affected by X-linked recessive disorders much more

frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one altered copy of the gene in each cell is called a carrier. She can pass on the gene, but generally does not experience signs and symptoms of the disorder. In rare cases, however, carrier females have shown some retinal abnormalities or mild hearing loss associated with Norrie disease.

Other Names for This Condition

- Anderson-Warburg syndrome
- Atrophia bulborum hereditaria
- congenital progressive oculo-acoustico-cerebral degeneration
- Episkopi blindness
- Fetal iritis syndrome
- Norrie syndrome
- Norrie-Warburg syndrome
- Norrie's disease
- Oligophrenia microphthalmus
- pseudoglioma congenita
- Whitnall-Norman syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Atrophia bulborum hereditaria
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0266526/

Other Diagnosis and Management Resources

- GeneReview: NDP-Related Retinopathies
  https://www.ncbi.nlm.nih.gov/books/NBK1331

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Eye Diseases
  https://medlineplus.gov/eyediseases.html

Genetic and Rare Diseases Information Center

- Norrie disease
  https://rarediseases.info.nih.gov/diseases/7224/norrie-disease

Educational Resources

- Disease InfoSearch: Norrie disease
  http://www.diseaseinfosearch.org/Norrie+disease/5270
- MalaCards: norrie disease
  http://www.malacards.org/card/norrie_disease
- Orphanet: Norrie disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=649

Patient Support and Advocacy Resources

- Foundation Fighting Blindness
  http://www.blindness.org/
- Helen Keller National Center for Deaf-Blind Youths and Adults
  https://www.helenkeller.org/hknc
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/norrie-disease/

GeneReviews

- NDP-Related Retinopathies
  https://www.ncbi.nlm.nih.gov/books/NBK1331

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22norrie+disease%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28norrie+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- NORRIE DISEASE
  http://omim.org/entry/310600

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