Subcortical band heterotopia

Description

Subcortical band heterotopia is a condition in which nerve cells (neurons) do not move (migrate) to their proper locations in the fetal brain during early development. (Heterotopia means "out of place.") Normally, the neurons that make up the outer surface of the brain (cerebral cortex) are distributed in a well-organized and multi-layered way. In people with subcortical band heterotopia, some neurons that should be part of the cerebral cortex do not reach it. These neurons stop their migration process in areas of the brain where they are not supposed to be and form band-like clusters of tissue. Since these bands are located beneath the cerebral cortex, they are said to be subcortical. In most cases, the bands are symmetric, which means they occur in the same places on the right and left sides of the brain.

The abnormal brain development causes neurological problems in people with subcortical band heterotopia. The signs and symptoms of the condition depend on the size of the bands and the lack of development of the cerebral cortex. The signs and symptoms can vary from severe intellectual disability and seizures that begin early in life and affect both sides of the brain (generalized seizures) to normal intelligence with seizures occurring later in life and affecting only one side of the brain (focal seizures). Some affected individuals also have weak muscle tone (hypotonia), loss of fine motor skills such as using utensils, or behavioral problems. Subcortical band heterotopia is typically found when brain imaging is done following the onset of seizures, usually in adolescence or early adulthood.

Frequency

More than 200 cases of subcortical band heterotopia have been reported in the scientific literature. Most affected individuals are female.

Causes

Mutations in the *DCX* or *PAFAH1B1* gene cause subcortical band heterotopia. Both genes provide instructions for making proteins that are involved in the movement of neurons to their proper locations in the developing brain, a process called neuronal migration. Neuronal migration is essential for normal brain development and function.

Most individuals with subcortical band heterotopia have *DCX* gene mutations. These

mutations impair the protein's function or alter the protein's structure or stability. *PAFAH1B1* gene mutations are less common. Mutations in this gene reduce the protein's function.

Altered structure or function of the proteins produced by the *DCX* or *PAFAH1B1* gene impairs important interactions that are needed for neuronal migration. Without proper neuronal migration, neurons in the developing brain can be misplaced, forming abnormal bands of tissue beneath the cerebral cortex.

Learn more about the genes associated with Subcortical band heterotopia

- DCX
- PAFAH1B1

Inheritance

The inheritance pattern of subcortical band heterotopia depends on its genetic cause.

When subcortical band heterotopia is caused by mutations in the *DCX* gene, it is inherited in an X-linked pattern. The *DCX* gene is located on the X chromosome, which is one of the two sex chromosomes. In females, who have two copies of the X chromosome, one altered copy of the gene in each cell can lead to the condition, sometimes with less severe symptoms than affected males. In males, who have only one X chromosome, a mutation in the only copy of the gene in each cell usually causes a more severe condition called isolated lissencephaly sequence (ILS). Most males with subcortical band heterotopia have a *DCX* gene mutation that is not inherited and is present in only some of the body's cells, a situation known as mosaicism. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

When subcortical band heterotopia is caused by a *PAFAH1B1* gene mutation, it is generally not inherited but arises from a mutation in the body's cells that occurs after conception, which leads to mosaicism. This alteration is called a somatic mutation. *PAFAH1B1* gene mutations that occur in all of the body's cells (germline mutations) usually cause ILS.

Other Names for This Condition

- DC syndrome
- Double cortex syndrome
- Heterotopia, subcortical band
- SBH
- SCLH
- Subcortical laminar heterotopia

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Subcortical band heterotopia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848201/)

Genetic and Rare Diseases Information Center

- Subcortical band heterotopia (https://rarediseases.info.nih.gov/diseases/1904/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Subcortical band heterotopia%22)

Catalog of Genes and Diseases from OMIM

- LISSENCEPHALY, X-LINKED, 1; LISX1 (https://omim.org/entry/300067)
- LISSENCEPHALY 1; LIS1 (https://omim.org/entry/607432)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28subcortical+band+heterotopia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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