CYLD cutaneous syndrome

Description

CYLD cutaneous syndrome is a genetic condition characterized by the growth of multiple noncancerous (benign) skin tumors. These tumors develop from structures associated with the skin (skin appendages), such as hair follicles. More than one type of skin tumor often develops, including benign growths called cylindromas, spiradenomas, and trichoepitheliomas. Cylindromas were previously thought to derive from sweat glands, but they are now generally believed to begin in hair follicles and often appear on the scalp. Spiradenomas are related to cylindromas and it is common to find features of both of these benign growths in a single tumor. Trichoepitheliomas arise from hair follicles and typically develop on the skin around the nose and upper lip.

While the skin tumors associated with *CYLD* cutaneous syndrome are typically benign, occasionally they may become cancerous (malignant). When becoming malignant, tumors often grow rapidly and become open sores (ulcers). Affected individuals are also at increased risk of developing tumors in structures other than skin; for example benign or malignant tumors of the salivary glands occur in some people with the condition.

People with *CYLD* cutaneous syndrome typically begin developing tumors in late childhood or in their teens. For reasons that are unclear, females with *CYLD* cutaneous syndrome tend to develop more tumors than males with this condition. Tumors tend to grow larger and increase in number over time. Large benign tumors may become ulcers and prone to infections. The tumors are most often found on the head and neck, including the scalp. Tumors that occur in the eyes, ears, nose, or mouth can affect the senses, including vision and hearing. Less frequently, tumors develop on the torso, armpits, or genitals. Genital tumors may cause pain and sexual dysfunction. Rarely, cylindromas develop in the airways and can cause problems with breathing (respiratory insufficiency).

The tumors in *CYLD* cutaneous syndrome can be disfiguring and may contribute to depression or other psychological problems.

CYLD cutaneous syndrome includes the conditions previously called Brooke-Spiegler syndrome, multiple familial trichoepithelioma, and familial cylindromatosis. These conditions were once thought to be distinct disorders but are now considered to be the same condition.

Frequency

The prevalence of *CYLD* cutaneous syndrome is unknown, but the condition is estimated to affect more than 1 in 100,000 individuals. More than 100 affected families have been reported in the scientific literature.

Causes

CYLD cutaneous syndrome is caused by mutations in the *CYLD* gene. The *CYLD* gene provides instructions for making an enzyme that helps regulate numerous signaling pathways, many of which are involved in cell growth. By regulating these signaling pathways, the CYLD enzyme helps cells respond properly to signals that promote cell growth and division (proliferation) or self-destruction (apoptosis), as necessary. The CYLD enzyme acts as a tumor suppressor, which means that it helps prevent cells from growing and dividing too fast or in an uncontrolled way

People with *CYLD* cutaneous syndrome are born with a mutation in one of the two copies of the *CYLD* gene in each cell. This mutation prevents the cell from making functional CYLD enzyme from the altered copy of the gene. However, enough enzyme is usually produced from the remaining, normal copy of the gene to regulate cell growth effectively. For tumors to develop, a second mutation that alters or removes (deletes) the normal copy of the *CYLD* gene must occur. The second mutation, called a somatic mutation, occurs during a person's lifetime and is found in only certain cells in the body.

When both copies of the *CYLD* gene are mutated, the cell cannot produce any functional CYLD enzyme. The loss of this enzyme allows the cell to grow and divide in an uncontrolled way to form a tumor. In people with *CYLD* cutaneous syndrome, a second *CYLD* gene mutation typically occurs in multiple cells over an affected person's lifetime. The loss of CYLD enzyme in different types of cells, especially those in structures in the skin, leads to the growth of a variety of tumors.

Learn more about the gene associated with CYLD cutaneous syndrome

- CYLD

Inheritance

Susceptibility to *CYLD* cutaneous syndrome has an autosomal dominant pattern of inheritance, which means one copy of the altered *CYLD* gene in each of the body’s cells increases the risk of developing this condition. The initial genetic change is known as a germline mutation, which most individuals with this condition inherit from a parent. A second, somatic mutation is required for development of tumors in *CYLD* cutaneous syndrome. Depending when the second mutation occurs, the benign tumors may be clustered to one side of the body or face.

Rarely, the first *CYLD* gene mutation is not inherited but is a somatic mutation that occurs early in development. As a result, some of the body's cells have a normal

version of the gene, while others have the mutated version. This situation is called mosaicism. As in inherited cases, a second somatic mutation in the normal copy of the gene later in life is required for tumors to develop. These cases of *CYLD* cutaneous syndrome are not inherited and typically occur in people with no history of the disorder in their family.

Other Names for This Condition

- CCS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Brooke-Spiegler syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1857941/)

Genetic and Rare Diseases Information Center

- Brooke-Spiegler syndrome (https://rarediseases.info.nih.gov/diseases/10179/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- CYLINDROMATOSIS, FAMILIAL (https://omim.org/entry/132700)
- TRICHOEPITHELIOMA, MULTIPLE FAMILIAL, 1 (https://omim.org/entry/601606)
- BROOKE-SPIEGLER SYNDROME; BRSS (https://omim.org/entry/605041)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=CYLD+cutaneous+syndrome&sort=date)

References

- Arefi M, Wilson V, Muthiah S, Zwolinski S, Bajwa D, Brennan P, Blasdale K,Bourn D, Burn J, Santibanez-Koref M, Rajan N. Diverse presentations of cutaneousmosaicism occur in CYLD cutaneous syndrome and may result in parent-to-childtransmission. J Am Acad Dermatol. 2019 Dec;81(6):1300-1307. doi:10.1016/j.jaad.2019.05.021. Epub 2019 May 11. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31085270)

- Arruda AP, Cardoso-Dos-Santos AC, Mariath LM, Feira MF, Kowalski TW, BezerraKRF, da Silva LACT, Ribeiro EM, Schuler-Faccini L. A large family with CYLDcutaneous syndrome: medical genetics at the community level. J Community Genet.2020 Jul;11(3):279-284. doi: 10.1007/s12687-019-00447-2. Epub 2019 Dec 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31792733)
- Brown SM, Arefi M, Stones R, Loo PS, Barnard S, Bloxham C, Stefanos N, LangtryJAA, Worthy S, Calonje E, Husain A, Rajan N. Inherited pulmonary cylindromas:extending the phenotype of CYLD mutation carriers. Br J Dermatol. 2018Sep;179(3):662-668. doi: 10.1111/bjd.16573. Epub 2018 May 29. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29569226)
- Dubois A, Rajan N. CYLD Cutaneous Syndrome. 2020 Apr 16. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK555820/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/32298062)
- Dubois A, Wilson V, Bourn D, Rajan N. CYLD GeneticTesting for Brooke-SpieglerSyndrome, Familial Cylindromatosis and Multiple Familial Trichoepitheliomas. PLoSCurr. 2015 Feb 19;7:ecurrents.eogt. 45c4e63dd43d62e12228cc5264d6a0db. doi:10.1371/currents.eogt. 45c4e63dd43d62e12228cc5264d6a0db. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25737804)
- Rajan N, Ashworth A. Inherited cylindromas: lessons from a rare tumour. LancetOncol. 2015 Sep;16(9):e460-e469. doi: 10.1016/S1470-2045(15)00245-4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26370355)
- Rito M, Mitani Y, Bell D, Mariano FV, Almalki ST, Pytynia KB, Fonseca I,El-Naggar AK. Frequent and differential mutations of the CYLD gene in basal cellsalivary neoplasms: linkage to tumor development and progression. Mod Pathol.2018 Jul;31(7):1064-1072. doi: 10.1038/s41379-018-0018-6. Epub 2018 Feb 20. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29463883)

Last updated December 16, 2020