Multiple familial trichoepithelioma

Multiple familial trichoepithelioma is a condition involving multiple skin tumors that develop from structures associated with the skin (skin appendages), such as hair follicles and sweat glands. People with multiple familial trichoepithelioma typically develop large numbers of smooth, round tumors called trichoepitheliomas, which arise from hair follicles. Trichoepitheliomas are generally noncancerous (benign) but occasionally develop into a type of skin cancer called basal cell carcinoma.

Individuals with multiple familial trichoepithelioma occasionally also develop other types of tumors, including growths called spiradenomas and cylindromas. Spiradenomas develop in sweat glands. The origin of cylindromas has been unclear; while previously thought to derive from sweat glands, they are now generally believed to begin in hair follicles. Affected individuals are also at increased risk of developing tumors in tissues other than skin appendages, particularly benign or malignant tumors of the salivary glands.

People with multiple familial trichoepithelioma typically begin developing tumors during childhood or adolescence. The tumors mostly appear on the face, especially in the folds in the skin between the nose and lips (nasolabial folds, sometimes called smile lines), but may also occur on the neck, scalp, or trunk. They may grow larger and increase in number over time.

In severe cases, the tumors may get in the way of the eyes, ears, nose, or mouth and affect vision, hearing, or other functions. The growths can be disfiguring and may contribute to depression or other psychological problems. For reasons that are unclear, females with multiple familial trichoepithelioma are often more severely affected than males.

Frequency

Multiple familial trichoepithelioma is a rare disorder; its prevalence is unknown.

Causes

Multiple familial trichoepithelioma can be caused by mutations in the CYLD gene. This gene provides instructions for making a protein that helps regulate nuclear factor-kappa-B. Nuclear factor-kappa-B is a group of related proteins that help protect cells from self-destruction (apoptosis) in response to certain signals. In regulating the action of nuclear factor-kappa-B, the CYLD protein allows cells to respond properly to signals to self-destruct when appropriate, such as when the cells become abnormal. By this mechanism, the CYLD protein 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 \textit{CYLD}-related multiple familial trichoepithelioma are born with a mutation in one of the two copies of the \textit{CYLD} gene in each cell. This mutation prevents the cell from making functional CYLD protein from the altered copy of the gene. However, enough protein is usually produced from the other, normal copy of the gene to regulate cell growth effectively. For tumors to develop, a second mutation or deletion of genetic material involving the other copy of the \textit{CYLD} gene must occur in certain cells during a person's lifetime.

When both copies of the \textit{CYLD} gene are mutated in a particular cell, that cell cannot produce any functional CYLD protein. The loss of this protein allows the cell to grow and divide in an uncontrolled way to form a tumor. In people with multiple familial trichoepithelioma, a second \textit{CYLD} mutation typically occurs in multiple cells over an affected person's lifetime. The loss of CYLD protein in these cells leads to the growth of skin appendage tumors.

Some researchers consider multiple familial trichoepithelioma and two related conditions called familial cylindromatosis and Brooke-Spiegler syndrome, which are also caused by \textit{CYLD} gene mutations, to be different forms of the same disorder. It is unclear why mutations in the \textit{CYLD} gene cause different patterns of skin appendage tumors in each of these conditions, or why the tumors are generally confined to the skin in these disorders.

Some people with multiple familial trichoepithelioma do not have mutations in the \textit{CYLD} gene. Scientists are working to identify the genetic cause of the disorder in these individuals.

\textbf{Inheritance Pattern}

Susceptibility to multiple familial trichoepithelioma has an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell increases the risk of developing this condition. However, a second, non-inherited mutation is required for development of skin appendage tumors in this disorder.

\textbf{Other Names for This Condition}

- Brooke-Fordyce trichoepitheliomas
- EAC
- epithelioma adenoides cysticum of Brooke
- familial multiple trichoepitheliomata
- hereditary multiple benign cystic epithelioma
- MFT
Diagnosis & Management

Genetic Testing Information

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

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Benign Tumors https://medlineplus.gov/benigntumors.html
- Health Topic: Skin Conditions https://medlineplus.gov/skinconditions.html

Genetic and Rare Diseases Information Center

- Multiple familial trichoepithelioma https://rarediseases.info.nih.gov/diseases/10867/multiple-familial-trichoepithelioma

Educational Resources

- MalaCards: multiple familial trichoepithelioma https://www.malacards.org/card/multiple_familial_trichoepithelioma
- Orphanet: Familial multiple trichoepithelioma https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=867

Patient Support and Advocacy Resources

- AboutFace https://www.aboutface.ca/
- Skin Cancer Foundation https://www.skincancer.org/
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Skin+Neoplasms%5BMAJR%5D%29+AND+%28%28multiple+familial+trichoepithelioma%5BTIAB%5D%29+OR+%28mft%5BTIAB%5D%29+OR+%28epithelioma+adenoides+cysticum+of+brooke%5BTIAB%5D%29+OR+%28eac%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- TRICHOEPITHELIOMA, MULTIPLE FAMILIAL, 1
  http://omim.org/entry/601606

- TRICHOEPITHELIOMA, MULTIPLE FAMILIAL, 2
  http://omim.org/entry/612099

Sources for This Summary


  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735949/


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