Palmoplantar Keratoderma with Deafness

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Palmoplantar keratoderma with deafness is a disorder characterized by skin abnormalities and hearing loss.

Keywords: genetic conditions

1. Introduction

Affected individuals develop unusually thick skin on the palms of the hands and soles of the feet (palmoplantar keratoderma) beginning in childhood. Hearing loss ranges from mild to profound. It begins in early childhood and gets worse over time. Affected individuals have particular trouble hearing high-pitched sounds.

The signs and symptoms of this disorder may vary even within the same family, with some individuals developing only skin abnormalities and others developing only hearing loss.

2. Frequency

Palmoplantar keratoderma with deafness is a rare disorder; its prevalence is unknown. At least 10 affected families have been identified.

3. Causes

Palmoplantar keratoderma with deafness can be caused by mutations in the *GJB2* or *MT-TS1* genes.

The *GJB2* gene provides instructions for making a protein called gap junction beta 2, more commonly known as connexin 26. Connexin 26 is a member of the connexin protein family. Connexin proteins form channels called gap junctions that permit the transport of nutrients, charged atoms (ions), and signaling molecules between neighboring cells that are in contact with each other. Gap junctions made with connexin 26 transport potassium ions and certain small molecules.

Connexin 26 is found in cells throughout the body, including the inner ear and the skin. In the inner ear, channels made from connexin 26 are found in a snail-shaped structure called the cochlea. These channels may help to maintain the proper level of potassium ions required for the conversion of sound waves to electrical nerve impulses. This conversion is essential for normal hearing. In addition, connexin 26 may be involved in the maturation of certain cells in the cochlea. Connexin 26 also plays a role in the growth, maturation, and stability of the outermost layer of skin (the epidermis).

The *GJB2* gene mutations that cause palmoplantar keratoderma with deafness change single protein building blocks (amino acids) in connexin 26. The altered protein probably disrupts the function of normal connexin 26 in cells, and may interfere with the function of other connexin proteins. This disruption could affect skin growth and also impair hearing by disturbing the conversion of sound waves to nerve impulses.

Palmoplantar keratoderma with deafness can also be caused by a mutation in the *MT-TS1* gene. This gene provides instructions for making a particular type of RNA, a molecule that is a chemical cousin of DNA. This type of RNA, called transfer RNA (tRNA), helps assemble amino acids into full-length, functioning proteins. The *MT-TS1* gene provides instructions for a specific form of tRNA that is designated as $tRNA^{Ser(UCN)}$. This molecule attaches to a particular amino acid, serine (Ser), and inserts it into the appropriate locations in many different proteins.

The $tRNA^{Ser(UCN)}$ molecule is present only in cellular structures called mitochondria. These structures convert energy from food into a form that cells can use. Through a process called oxidative phosphorylation, mitochondria use oxygen, simple sugars, and fatty acids to create adenosine triphosphate (ATP), the cell's main energy source. The $tRNA^{Ser(UCN)}$ molecule is involved in the assembly of proteins that carry out oxidative phosphorylation.

The *MT-TS1* gene mutation that causes palmoplantar keratoderma with deafness leads to reduced levels of $tRNA^{Ser(UCN)}$ to assemble proteins within mitochondria. Reduced production of proteins needed for oxidative phosphorylation may impair the ability of mitochondria to make ATP. Researchers have not determined why the effects of the mutation are limited to cells in the inner ear and the skin in this condition.

The Genes Associated with Palmoplantar Keratoderma with Deafness

- GJB2
- MT-TS1

4. Inheritance

Palmoplantar keratoderma with deafness can have different inheritance patterns.

When this disorder is caused by *GJB2* gene mutations, it is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

When palmoplantar keratoderma with deafness is caused by mutations in the *MT-TS1* gene, it is inherited in a mitochondrial pattern, which is also known as maternal inheritance. This pattern of inheritance applies to genes contained in mitochondrial DNA (mtDNA). Because egg cells, but not sperm cells, contribute mitochondria to the developing embryo, children can only inherit disorders resulting from mtDNA mutations from their mother. These disorders can appear in every generation of a family and can affect both males and females, but fathers do not pass traits associated with changes in mtDNA to their children.

5. Other Names for This Condition

- palmoplantar hyperkeratosis-deafness syndrome
- palmoplantar hyperkeratosis-hearing loss syndrome
- palmoplantar keratoderma-deafness syndrome
- palmoplantar keratoderma-hearing loss syndrome
- PPK with deafness
- PPK-deafness syndrome

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