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My46 Trait Profile

Nonsyndromic congenital hearing loss

Other Names: nonsyndromic congenital deafness, nonsyndromic pre-lingual hearing loss/deafness

Congenital hearing loss is hearing below standard levels for normal hearing that is present at birth. Approximately 50% of congenital hearing loss is due to genetic factors. The majority of genetic congenital hearing loss is caused by mutations in the GJB2 gene that makes the connexin 26 protein.

Characteristics of Nonsyndromic congenital hearing loss

Congenital hearing loss is a common and complicated permanent condition affecting approximately 1 in 500 individuals. Congenital hearing loss or deafness is present at birth, and therefore before a child learns to speak (prelingual). Over 50% of congenital hearing loss is caused by genetic factors such as changes or mutations in single genes, chromosomal problems, or combinations of genetic and environmental factors (multifactorial conditions). The remainder is due to environmental causes such as viral infection (i.e. cytomegaolovirus), exposure to medications that can cause hearing loss, accidents or trauma to the head or ear, etc.

Congenital hearing loss in individuals with additional physical features is referred to as syndromic hearing loss. Syndromic hearing loss represents approximately 30% of congenital hearing loss due to genetic factors. Over 400 syndromes that include hearing loss have been described (e.g., Down syndrome). The remaining 70% of genetic congenital hearing loss (or 35% of all congenital hearing loss) is nonsyndromic (not associated with additional features) or isolated. These nonsyndromic forms of congenital hearing loss may be inherited in a variety of ways. Approximately 80% of the nonsyndromic forms of congenital hearing loss are caused by mutations in autosomal recessive genes, 20% are caused by mutations in autosomal dominant genes, 1% in X-linked genes, and

Hearing loss can be classified or distinguished in many ways such as by the severity of the loss (mild, moderate, severe or profound), progression (hearing loss that becomes more severe over time), vestibular involvement (involvement of the balance center in the brain), the type of loss (conductive - caused by a blockage, usually in the outer ear, that prevents sound from reaching the inner ear; or sensorineural - caused by abnormalities to the inner ear or cochlea, or to the nerve pathways from the inner ear to the brain; or both), and cause (genetic or environmental).

Diagnosis/Testing

The majority of nonsyndromic congenital hearing loss is due to mutations in the GJB2 gene. This gene makes a protein (connexin 26) that forms connections between cells. Mutations in this gene account for approximately 50% of all cases of nonsyndromic hearing loss. Over 100 mutations have been identified. Individuals who have GJB2 or connexin 26-related hearing loss typically have non-progressive, sensorineural hearing loss of congenital or prelingual onset, normal vestibular function, normal inner ear function, normal physical examination, and normal cognition or intelligence. The degree of hearing loss in affected individuals is variable. Connexin 26-related hearing loss is usually autosomal recessive and the carrier frequency of mutations may vary by ethnicity. Approximately 3.5% of Caucasians carry a mutation called c.35delG, 4% of individuals with Ashkenazi Jewish ancestry carry the c.167delT mutation, and the c.235delC is common in the Asian population. A few GJB2 mutations may result in autosomal dominant hearing loss and may also be associated with additional physical features.

Mutations in the GJB6 gene may also cause autosomal recessive or autosomal dominant, nonsyndromic hearing

loss. Many other genes that have been associated with nonsyndromic deafness include ATP2B2, ACTG1, CDH23, CLDN14, COCH, COL11A2, DFNA5, DFNB31, DFNB59, ESPN, EYA4, GJB3, KCNQ4, LHFPL5, MYO1A, MYO15A, MYO6, MYO7A, OTOF, PCDH15, POU3F4, SLC26A4, STRC, TECTA, TMC1, TMIE, TMPRSS3, TRIOBP, USH1C, and WFS1.

Many babies with congenital hearing loss are identified early in life through newborn screening (in the United States). However, this screening frequently does not identify the cause or etiology of the hearing loss.

Management/Surveillance

Individuals with congenital hearing loss are usually managed by a team of specialty providers that can include clinical geneticists, genetic counselors, otolaryngologists (ENTs), audiologists, speech and language specialists, primary care doctors, and other appropriate specialists as needed. Referral to a pediatric ENT is always indicated.

Early intervention has been shown to be effective in facilitating speech and language development in children with hearing loss therefore, enrollment in early intervention services is recommended.

Mode of inheritance

Nonsyndromic congenital hearing loss may be inherited in a variety of ways including autosomal recessive, autosomal dominant, X-linked, and mitochondrial patterns.

Autosomal recessive inheritance:

The most frequent cause of nonsyndromic congenital hearing loss is due to mutations in the GJB2 gene which is inherited in an autosomal recessive pattern. This means that an individual has to inherit two GJB2 mutations (i.e., one from each parent) to be affected with GJB2-related nonsyndromic congenital hearing loss. If both parents are carriers of a GJB2 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with GJB2-related nonsyndromic congenital hearing loss.

Autosomal dominant inheritance:

Some individuals with congenital hearing loss may have mutations in the GJB2 or GJB6 genes that can also cause autosomal dominant hearing loss. This means inheriting one of these GJB2 or GJB6 mutations is enough for an individual to have hearing loss. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Risk to family members

Risks to family members are dependent on the inheritance pattern associated with the type of hearing loss in the family.

Autosomal recessive inheritance:

Parents of a child with GJB2-related autosomal recessive hearing loss are carriers of this same type of hearing loss. If a sibling of a child with GJB2-related hearing loss is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of the condition.

Autosomal dominant inheritance:

The risk to family members of autosomal dominant hearing loss depends on whether or not the individual hearing loss has a parent also affected with this kind of hearing loss. If a parent also has the condition, the risk of having a child with autosomal dominant hearing loss is 50% with each pregnancy. If a parent does not have the condition, the risk of other siblings being affected is very low.

Special considerations

None

Resources

American Speech-Language-Hearing Association
http://www.asha.org/
Genetics Home Reference: nonsyndromic deafness
http://ghr.nlm.nih.gov/condition/nonsyndromic-deafness
Hearing Loss Association of America
http://www.hearingloss.org/

My baby's hearing
http://www.babyhearing.org/
National Center for Hearing Assessment and Management
http://www.infanthearing.org/

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