

Inherited Hearing Loss

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(return visit of case 10, seven months later)

Key Points

- DFNB1 is an autosomal recessive condition characterized by congenital, usually nonprogressive, sensorineural hearing impairment.
- The diagnosis of DFNB1 is made if an individual has disease-causing mutations in the *GJB2* gene that alters the connexin 26 (Cx26) protein.
- Making this diagnosis does not alter treatment but can alter further diagnostic evaluation(s) and enables families to more accurately determine the risk of having future offspring with deafness.

Learning Objectives

Participants will be able to:

- Describe the clinical findings in individuals with DFNB1;
- Explain the possible molecular genetic test results associated with DFNB1.

Family History Issues

An affected individual may have a family history of deafness consistent with autosomal recessive inheritance (for example, an affected sibling). However, the majority of people with autosomal recessive conditions represent the first known case in their family. It is also possible for an individual with autosomal recessive hearing loss to have deaf parent(s) who also have an autosomal recessive hearing loss, leading to the appearance of a "pseudo" dominant family history.

Red Flags



Possible signs of DFNB1 include nonsyndromic, sensorineural hearing loss that is consistent with autosomal recessive inheritance.

Case 11. Parents Seek Reproductive Counseling Following the Diagnosis of DFNB1-Related Hearing Loss in Their Son

Mr. and Mrs. W come in with Scott, who was found to have hearing loss in the newborn period, and is now seven months old. His hearing loss has been diagnosed as DFNB1, based on a genetic test identifying two mutations in the *GJB2* gene. He has been doing well with speech and hearing therapy. The family is considering cochlear implants for him. They want to discuss with you what they have learned from the subspecialists they have seen, and they have questions about whether they should get prenatal testing with their next pregnancy.

Clinical Care Issues

DFNB1 is an autosomal recessive condition characterized by congenital, usually nonprogressive, sensorineural hearing impairment. In most cases the hearing impairment is severe or severe to profound; however, it can range from mild to severe in different families and within a family. Except for the hearing impairment, affected individuals are healthy and enjoy a normal life span. Vestibular function is normal; affected infants and young children do not experience balance problems and learn to sit and walk at age-appropriate times.

DFNB1-related hearing loss is suspected in individuals who have (1) congenital, nonprogressive sensorineural hearing impairment that is mild to profound by auditory brainstem response testing (ABR) or pure tone audiometry; (2) no related systemic findings identified by medical history or physical examination. They may also have a family history consistent with autosomal recessive inheritance of hearing loss (for example, an affected sibling). However, the majority of people with autosomal recessive conditions represent the first known case in their family.

The diagnosis of DFNB1 is confirmed if the individual has recognized disease-causing mutations in the *GJB2* gene that alter the connexin 26 (Cx26) protein. Full DNA sequencing of the *GJB2* gene detects two identifiable mutations in about 98% of individuals with DFNB1. The most common mutation, 35delG, is found in over two-thirds of persons with DFNB1, but at least 80 other disease-causing mutations have been identified. The

remaining 2% of individuals with DFNB1 have one identifiable *GJB2* mutation and a large deletion in the adjacent chromosomal region including a portion of *GJB6*, a gene adjacent to *GJB2* that encodes the connexin 30 (Cx30) protein. It is likely that this deletion affects the upstream regulatory regions of *GJB2*, which, when combined with the *GJB2* mutation in the coding region of the other allele, results in lack of production of connexin 26. (See [GeneReview: DFNB1, Summary](#) for further information.)

Risk Assessment

DFNB1 is inherited in an autosomal recessive manner. Since Scott has two identifiable mutations in *GJB2*, both of his parents are obligate carriers of a mutation in *GJB2*. For future pregnancies, there is a 25% risk of inheriting a mutation from each parent, thus having DFNB1 with hearing loss.

Scott's three-year-old sister has undergone a hearing evaluation and does not exhibit any hearing loss, which confirms that she does not have DFNB1 and therefore did not inherit two mutations in *GJB2*. However, she has a 2/3 risk of being a carrier of one mutation in *GJB2*.

The risk to Scott's aunts and uncles of being carriers of a *GJB2* mutation is 50%.

Genetic Counseling and Testing

The genetic diagnosis of DFNB1 may have implications for reproductive decision making. Parents may take into consideration the risk of having a child with hearing loss when deciding whether to have more children. Additionally, DFNB1 can be diagnosed in utero. Prenatal testing is available for couples at 25% risk of having a child with DFNB1 and in whom the disease-causing mutations are known. DNA extracted from cells obtained from amniocentesis at 16-18 weeks' gestation or chorionic villus sampling (CVS) at 10-12 weeks' gestation can be analyzed. Genetic counseling can assist families in determining the role of genetic testing or knowledge of genetic risk in their lives.

Carrier detection may be relevant in the reproductive counseling of other relatives of an affected individual. DNA-based testing can only be considered if the disease-causing mutations have been identified in an affected family member. Subsequently, the relatives at risk of being carriers can be tested for these mutations using the same laboratory techniques.

Interventions

For all types of hearing loss, early interventions with speech and hearing therapy are considered to be essential. Treatment for sensorineural hearing loss depends on the severity of the loss and also on parental choice.

Amplification through hearing aids is used in the majority of cases; cochlear implantation is a possibility for children with bilateral severe to profound hearing loss. Nonrandomized, prospective studies have demonstrated superior communication performance in children with prelingual deafness who received cochlear implants as compared to similar children using more traditional hearing aids.

Language development can also be fostered in profoundly deaf children through American Sign Language (ASL). The use of this approach without efforts at amplification may be preferred by parents (whether hearing or deaf) who are members of the Deaf community, which views deafness as a separate and valued culture in which members are bilingual (communicating in both ASL and English).

The diagnosis of DFNB1 implies that the child will have normal development and normal life span. It does not predict how this child would fare with a cochlear implant as compared to individuals with other sensorineural causes of profound hearing loss.

Ethical/Legal/Social/Cultural Issues

Adjusting to the diagnosis

It is important to ascertain and address the questions and concerns of the family/individual when they are considering genetic testing and receiving genetic test results. Families often want to know the cause of their child's hearing loss. Identification of a genetic cause may be comforting, because the certainty of a diagnosis is preferred over uncertainty and because it may relieve guilt: "Was it something I (we) did during the pregnancy that caused this?" Conversely, some parents feel guilt knowing that the child's condition was inherited from them. Confirming DFNB1 as the cause of a child's hearing loss can also provide reassurance to parents and health care providers that this child is not at risk of developing additional health concerns as can be seen in syndromic forms of hearing loss (e.g., Usher syndrome).

The parents may also wish to discuss with the physicians options for future


planning including cost of hearing devices, educational opportunities, and social acceptance or discrimination.

Deaf culture

Many deaf individuals are interested in obtaining information about the underlying etiology of their hearing loss rather than information about reproductive risks. Many do not consider themselves to be handicapped but define themselves as part of a distinct culture with its own language, customs, and beliefs. Genetic testing may thus sometimes provide an explanation for etiology rather than information for reproductive decision making.

Resources

- [American Academy of Pediatrics](#)
- [Boystown National Research Hospital: Resources for Parents](#)
- [American Society for Deaf Children](#)
PO Box 3355
Gettysburg, PA 17325
Phone: 717-334-7922 (business V/TTY); 800-942-ASDC (parent hotline)
Fax: 717-334-8808
Email: ASDC1@aol.com
- [National Association of the Deaf](#)
814 Thayer
Silver Spring, MD 20910
Phone: 301-587-1788 (voice); 301-587-1789 (TTY)
Fax: 301-587-1791
Email: NADinfo@nad.org
- [The Morton Hearing Research Group](#)
- [NCBI Genes and Disease Webpage: Deafness](#)

- [Hereditary Hearing Loss Homepage](#)
- [World Council on Hearing Health](#)
- [CDC Early Hearing Detection and Intervention Program \(EHDI\)](#)
- [National Center for Hearing Assessment and Management](#)
- [American Speech-Language-Hearing Association](#)
- [National Institute On Deafness and Other Communication Disorders](#)
- [Harvard Medical School Center for Hereditary Deafness brochure: Understanding the Genetics of Deafness: A Guide for Patients and Families](#)
- [National Library of Medicine Genetics Home Reference Nonsyndromic Deafness](#)
- [GeneTests Resources for DFNB1](#) 
- [GeneTests Online Medical Genetics Information Resource](#)

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