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Review Article

The Genetic Basis of Auditory Neuropathy Spectrum Disorder

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ABSTRACT

Introduction: Despite normal outer hair cell function, auditory neuropathy spectrum disorder (ANSD) disrupts neural coordination and impairs speech comprehension, especially in noisy environments.This review study explores the genetic mechanisms underlying ANSD.

Materials and Methods: PubMed, Scopus, and Web of Science were searched from 2010 to 2023 for studies on ANSD genetics, excluding those focused on non-genetic causes or lacking relevant data.

Results: ANSD is associated with conditions such as Brown-Vialetto-Van Laere syndrome (BVVL) and Charcot-Marie-Tooth (CMT) disease, often resulting from mutations in the auditory nerve. Nonsyndromic ANSD is associated with genes such as OTOF and PJVK, which are essential for neural function.

Conclusion: ANSD is a multifactorial condition resulting from genetic mutations in key genes, which disrupt auditory pathways and impair sound signal transmission. Further research is needed to identify additional genes and understand molecular mechanisms contributing to ANSD. This knowledge will improve diagnosis, prognosis, and therapeutic strategies, and could lead to innovative treatment approaches in the future.

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Introduction

Individuals with auditory neuropathy spectrum disorder often exhibit a notable discrepancy between their hearing thresholds, which may appear normal, and their difficulties with speech comprehension, particularly in noisy environments [1]. Terms like auditory neuropathy (AN) primarily describe this discrepancy, emphasizing the difficulty in understanding speech despite the ability to hear sounds [1]. Auditory desynchrony is another term for the primary issue: timing problems in neural transmission make it challenging to process sound information accurately. Auditory synaptopathy has recently emerged, focusing on potential dysfunctions at connections between inner hair cells and auditory nerve fibers, which can significantly impair auditory processing [2, 3].

Audiological findings in ANSD often reveal a unique pattern. Hearing loss, typically bilateral and sensorineural, can range from mild to severe, with a particular emphasis on lower frequencies. Audiograms may exhibit varied configurations, including peaked or saucer-shaped patterns [4]. Otoacoustic emissions are often preserved despite hearing loss, indicating that outer hair cell function is intact. On the other hand, auditory brainstem responses are usually absent or distorted, suggesting a disruption in neural transmission. The acoustic stapedial reflex is absent in most people with ANSD, further evidence that the brain is not working properly. Cochlear microphonics, which are often present, give more evidence of optimal outer hair cell function [5, 6].

While reported prevalence estimates range from less than 1% to 10% of individuals with hearing impairment [2], ANSD prevalence varies greatly, clearly depending on the specific population under study. Research indicates a higher prevalence among children with sensorineural hearing loss, especially those with severe-to-profound hearing impairment. The wide range in reported prevalence suggests that ANSD may be underdiagnosed in some populations [6-8].

ANSD can arise from various etiologies, including environmental and acquired factors. Some common non-genetic causes are early birth, high bilirubin levels, lack of oxygen, congenital brain defects, and exposure to drugs that damage the ears. If you have an acquired form of ANSD, you may start losing your hearing earlier than if you have a genetic form [9]. Genetic causes significantly influence the development of ANSD, with about 40% of cases having a genetic basis. There are different ways these genetic factors can be passed down, including autosomal dominant, autosomal recessive, X-linked, and mitochondrial inheritance [10]. Understanding the genetic basis of ANSD is essential for accurate diagnosis, effective treatment, the development of management strategies, such as gene therapy, and predicting disease progression. Genetic mutations can act as diagnostic markers, and comprehending genotype-phenotype correlations facilitates personalized medicine, ultimately enhancing patient outcomes. This study aims to investigate the role of genetics in the development of both syndromic and nonsyndromic ANSD and to analyze their related clinical and audiological manifestations.

Materials and Methods

A comprehensive search was conducted across PubMed, Scopus, and Web of Science from January 2010 to December 2023, using relevant keywords such as “auditory neuropathy spectrum disorder” and “genetics,” along with suitable variations, to identify studies related to the genetic aspects of ANSD. Boolean operators (AND, OR) refined the search strategy. This review included peer-reviewed articles that specifically addressed the genetic causes of ANSD, described the audiological characteristics associated with genetic conditions, and provided clinical profiles of individuals diagnosed with ANSD. Studies were excluded if they did not primarily focus on the genetic aspects of ANSD, did not include genetic information in their discussion of treatment options, lacked audiological data, or did not provide full-text access.

Results

We identified 52 articles spanning diverse case reports, case series, clinical reviews, genetic investigations, observational studies, and experimental research. These studies explore neurological and auditory disorders, examining genetic mutations, disease progression, clinical characteristics, and therapeutic interventions, providing valuable insights into both hereditary and acquired conditions affecting hearing and neural function. We will give the review results in greater detail by classifying the data into two main groups: syndromic and nonsyndromic variants. Each category will be examined thoroughly, highlighting the unique genetic pathways, crucial linked genes, and the clinical manifestations reported in both syndromic and nonsyndromic AN.

Syndromic

Brown-Vialetto-Van Laere syndrome (BVVL) is a rare neurodegenerative disorder that affects the sensorimotor nerves, the optic nerve, the bulbar nerve, and the lungs. Symptoms can include pontobulbar palsy, muscle weakness, and respiratory compromise. Patients may experience difficulties with feeding, hypotonia, and cranial nerve impairments. Magnetic resonance imaging can reveal abnormalities, such as T2 hyperintensity in the spinal cord. BVVL is primarily inherited in an autosomal recessive manner. Changes in the riboflavin transporter genes solute carrier family 52 member 2 (*SLC52A2*) and *SLC52A3* cause this syndrome. These genes encode riboflavin transporters, namely riboflavin transporter 2 (*RFVT2*) and riboflavin transporter 3 (*RFVT3*). There is evidence of genetic heterogeneity, with some cases suggesting a possible autosomal dominant pattern. Inheritance or involvement of a mutant gene on the X chromosome [11–13]. Audiological investigations in BVVLS patients typically reveal ANSD, with normal otoacoustic emissions but absent ABR, and the hearing loss in BVVLS is likely of postsynaptic origin [14].

Charcot-Marie-tooth (CMT) disease is the most common genetic neuromuscular condition, impacting approximately 1 in 2500 individuals [15]. It is characterized by peripheral nerve degeneration, leading to distal muscular weakness, atrophy, foot deformities, and sensory loss. CMT is genetically heterogeneous, with over 60 genes implicated in its pathogenesis. These genes are crucial for preserving neuronal integrity, facilitating axon transport, and enabling nerve signal transmission [16]. Key genes include peripheral myelin protein 22, myelin protein zero, gap junction protein beta 1, and SH3 domain-containing transcription factor 2 [17]. Research on hearing loss in CMT disease reveals a complex audiologic profile characterized by cochlear and neural deficits. Studies have found varying degrees of hearing loss, ranging from mild to severe, with difficulties in speech perception, especially in noisy environments. Audiological abnormalities include elevated or absent acoustic reflexes, abnormal ABR, and distorted otoacoustic emissions [18]. Hearing impairment in CMT patients is significant, with one study reporting that 28% of cases are affected [19]. AN appears to be present in all CMT type 4C patients, often detectable unilaterally in infancy and progressing with age. The hearing loss in CMT is generally bilateral and may be more severe in male patients [20].

Friedreich ataxia (*FRDA*) is an autosomal recessive neurodegenerative condition that mainly impacts the nervous system and heart. It is defined by decreased coordination and neurologic and cardiac complications [21]. The disease is caused by mutations in the *FRDA* gene, with 98% of cases due to guanine-adenine-adenine (GAA) trinucleotide repeat expansions in intron 1, leading to decreased frataxin protein levels [22]. Frataxin deficiency affects the muscular, nervous, and cardiovascular systems, leading to progressively worsening symptoms over time [23]. The pathogenesis involves mitochondrial iron accumulation, leading to increased free radical production and cellular damage [22]. *FRDA* is associated with auditory dysfunction, characterized by impaired temporal and spectral processing. Patients often exhibit sensorineural hearing loss and abnormal auditory brainstem responses [24]. The degree of auditory dysfunction correlates with the GAA trinucleotide repeat expansion, particularly when GAA1 exceeds 500 repeats. Auditory spatial processing deficits are also observed and may be linked to mild cognitive impairment in *FRDA* patients [25].

X-linked recessive ANSD is a hearing impairment primarily attributed to genetic mutations inherited in an X-linked recessive pattern. These mutations occur in the apoptosis-inducing factor gene (*AIFM1*), located on the X chromosome. *AIFM1* plays crucial roles in cellular processes, including programmed cell death and mitochondrial function. At the same time, while *AIFM1* mutations are associated with various disorders, including mitochondrial diseases with neurological and muscular manifestations, such as Cowchock syndrome, their involvement in X-linked recessive ANSD results explicitly in hearing impairment due to abnormalities within the auditory neural pathways. These mutations, often missense mutations that alter the protein's function, disrupt the normal functioning of *AIFM1*, leading to the characteristic hearing loss associated with this disorder. X-linked recessive ANSD is defined by variable hearing loss, ranging from mild to severe, with some individuals initially exhibiting normal hearing. Despite potentially normal outer hair cell function, as evidenced by standard otoacoustic emissions, abnormal auditory brainstem responses suggest that the primary issue lies in the neural conduction of the auditory signal to the brain. This late-onset condition, typically manifesting during adolescence, often spares female carriers of the *AIFM1* gene mutation, who usually have normal hearing, thus emphasizing this disorder's X-linked recessive inheritance pattern [26–28].

Kallmann syndrome (KS) is a genetic disorder described by hypogonadotropic hypogonadism and anosmia. KS results from impaired hypothalamic gonadotropin-releasing hormone secretion, leading to reduced sex hormone levels and delayed puberty. Recent research has identified five genes associated with KS: *KAL-1, FGFR1, PROKR2, PROK2,* and *NELF*. These genes have essential functions in the migration and maturation of olfactory and GnRH neurons. KS exhibits genetic heterogeneity, with autosomal dominant, autosomal recessive, and X-linked recessive inheritance patterns reported [29]. Studies have reported sensorineural hearing loss in KS patients; the auditory deficits in KS may be part of a broader spectrum of AN disorders. Genetic investigations have revealed mutations in genes such as *KAL1* as potential causes of KS with hearing loss. Additionally, radiological examinations have shown abnormal temporal bone anatomy and labyrinthine morphology in KS patients, which may contribute to both auditory and vestibular dysfunction [30–32].

CHARGE syndrome is a complex genetic disorder identified by a specific pattern of congenital anomalies, including coloboma, heart defects, choanal atresia, growth retardation, genital hypoplasia, and ear abnormalities. The syndrome is primarily due to mutations in the chromodomain helicase DNA-binding protein 7 (*CHD7*) gene on chromosome 8q12.1. Individuals with *CHD7* mutations are more frequently associated with ocular colobomas, temporal bone abnormalities, and facial nerve paralysis than those without [33–35]. CHARGE syndrome is related to various auditory abnormalities, including sensorineural hearing loss and AN. Patients often have hypoplastic or absent auditory nerves, which can affect cochlear implant outcomes. Temporal bone abnormalities, such as ossicular deformities and cochlear malformations, are common [36].

Sotos syndrome is a rare genetic disorder defined by abnormal growth, distinctive facial features, macrocephaly, and varying degrees of learning difficulties. The condition is primarily due to mutations or deletions in the nuclear receptor-binding SET domain protein 1 (SETD1), located on chromosome 5q35, which encodes a histone methyltransferase involved in transcriptional regulation. Associated features may include hypotonia, feeding difficulties, seizures, and an increased risk of tumors [37, 38]. It is related to various otolaryngologic manifestations. At the same time, conductive hearing loss and chronic otitis media are commonly reported. ANSD has been observed in conjunction with Sotos syndrome [19, 39].

CAPOS syndrome is an uncommon inherited neurological condition resulting from mutations in the *ATP1A3* gene, specifically the c.2452G>A (p.Glu818Lys) variant. The syndrome is defined by cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss, typically triggered by febrile episodes in childhood. Patients may experience recurrent acute ataxic encephalopathy, with symptoms improving within days but showing slow progression afterward [40, 41]. CAPOS syndrome is associated with AN spectrum disorder. This rare condition presents with intact outer hair cell activity with impaired neural synchronization along the auditory pathway. Audiological evaluations typically show preserved otoacoustic emissions and cochlear microphonics but abnormal auditory brainstem responses. Patients often experience poor speech perception, especially in noisy environments [42, 43].

Nonsyndromic

Some mutations in the *OTOF* gene are linked to a condition called nonsyndromic recessive AN, which affects the auditory pathway but not the outer hair cells. This condition results in varying degrees of hearing impairment, as evidenced by the presence of otoacoustic emissions in some patients, indicating intact OHC function and distinguishing it from other forms of hearing loss. The *OTOF* gene is important for AN because it encodes a protein required for the function of inner hair cells in the cochlea. This protein affects the release of neurotransmitters and the transmission of auditory signals [45]. New *OTOF* mutations and their varying frequencies in AN have been found in studies involving a wide range of populations. In Taiwan, a new *p.E1700Q* mutation was found in 23% of AN families, suggesting a possible founder effect [45]. Six new pathogenic variants were found in research from Brazil. *OTOF* mutations were found in 7.7% of cases of autosomal recessive hearing loss and were more common in the AN cases [46]. Italian studies identified 5 new OTOF mutations in children with AN, further solidifying the gene's role in this condition [47]. A new homozygous frameshift mutation (*c.1981dupG*) in the *OTOF* gene was also found to be the reason why one Iranian family had trouble hearing [48].

Changes in the *PJVK* gene, which encodes pejvakin, cause DFNB59, an autosomal recessive nonsyndromic hearing loss with variable symptoms. A Pakistani family with *p.C343S* [49] and a Chinese family with *c.930_931del AC* both have new mutations [50]. Other mutations found in Spanish cases are *p.Leu224Arg, p.His294Ilefs*43, p.His294Asp, and p.Phe317Serfs*20*. *PJVK* mutations can result in both cochlear dysfunction and ANSD. Patients with *PJVK* mutations typically demonstrated severe to profound hearing impairment [51].

Changes in the *TMC1* gene are associated with two types of hearing loss that do not exhibit any other symptoms: Autosomal recessive (DFNB7/11) and autosomal dominant (DFNA36). DFNB7/11 typically results in congenital or prelingual severe-to-profound hearing loss, while DFNA36 causes post-lingual, progressive hearing loss. *TMC1* mutations disrupt mechanical-to-electrical conversion in inner ear hair cells. Studies have identified novel mutations in different populations, including 4 in Turkish families and 5 in other families. Interestingly, some *TMC1* mutations can cause moderate to severe hearing loss rather than profound deafness, which suggests that the protein still functions [52–54].

The *DIAPH3* gene has been recognized as the cause of autosomal dominant nonsyndromic AN. A change in *DIAPH3*'s 5' UTR leads to the overexpression of the protein, resulting in hearing loss in humans and Drosophila [55]. A new frameshift variant, *c.3551_3552del* (*p.Glu1184AlafsTer11*), was identified in the DIAPH1 gene in a separate study. This change, located in exon 26 within a linkage region with a high LOD score, is associated with AN in the studied family, strongly suggesting that it contributes to the observed hearing impairment phenotype [56].

Mutations in the *OPA1* gene, primarily associated with dominant optic atrophy, can also cause AN and vestibular dysfunction. Studies have identified specific mutations, such as *R445H*, that cause deafness by impairing the function of auditory nerve terminals. The *Opa1delTTAG* mouse model exhibited adult-onset progressive AN, characterized by the breakdown of spiral ganglion neuron fibers and loss of inner hair cells. A review of 327 patients with *OPA1* mutations revealed that 6.4% experienced sensorineural hearing loss, with varying onset ranging from childhood to adulthood. Audiological tests often support the diagnosis of AN in these cases [57–59].

A new type of autosomal-dominant auditory synaptopathy/neuropathy called AUNA2 has been found in a German family. It was first linked to chromosomes 12q24 and 13q34. AUNA2 is characterized by slowly progressive post-lingual hearing loss, accompanied by no additional symptoms [60].

GJB2 gene mutations are the main cause of nonsyndromic sensorineural hearing loss (NSHL) across various populations. Studies in Chinese patients have identified several mutations, with *235delC* being the most prevalent. The mutation spectrum differs between ethnic groups, with *235delC* more common in East Asian populations than *35delG*, which is prevalent in Caucasians [61]. *GJB2* mutations can cause both autosomal recessive and dominant forms of NSHL. Some *GJB2* mutations also lead to persistent skin and hearing problems, which typically follow a dominant inheritance pattern [62]. A study found no significant correlation between ANSD and *GJB2* mutations, with only 7.5% of ANSD patients harboring *GJB2* mutations [63]. Recently, however, 16 of the 117 people with ANSD studied had *GJB2* mutations. This finding suggests that *GJB2* variants may be deleterious in ANSD [64].

Treatment options for ANSD

This section provides a brief overview of current treatment strategies, and a more comprehensive discussion of treatment options for ANSD is beyond the scope of this review. The treatment of ANSD currently focuses on maximizing auditory function through a multidisciplinary approach. Hearing aids are the primary treatment for mild to moderate hearing loss. Also, people with severe to profound hearing loss are thought to be getting cochlear implants. This condition is especially true if the inner hair cells do not function correctly or if hearing aids do not provide significant relief. Careful patient counseling, considering individual needs and expectations, is essential in selecting the most appropriate amplification strategy. FM-listening systems can significantly improve signal-to-noise ratios in challenging listening environments, enhancing speech understanding. Gene therapy holds tremendous promise for the future of ANSD treatment. New methods, such as CRISPR-Cas9, SMaRT, and AAV-mediated gene therapy, are being used to correct underlying genetic changes, stimulate the growth of new auditory synapses, and restore the nerves that control hearing. Early preclinical and clinical trials have yielded promising results, but further research is needed to address challenges, including developing accurate animal models, refining diagnostic tools, and assessing the drug's long-term safety and efficacy. Gene therapy products, such as DB-OTO and OTOF-GT, approved by the FDA, represent a significant step forward in the search for effective, targeted treatments for genetic forms of ANSD [65, 66].

Discussion

ANSD is a complex, multifactorial condition arising from various genetic causes and occurring in both syndromic and nonsyndromic forms. Recent genetic studies have highlighted mutations in several key genes, including *OTOF, PJVK, TMC1, DIAPH3,* and *OPA1*, which significantly contribute to the development of this disorder. These genetic changes can disrupt the normal

functioning of auditory pathways, resulting in impaired transmission of sound signals from the inner ear to the brain, even when the outer hair cells remain intact.

Given the diversity and complexity of these genetic disorders, further research is needed to identify additional genes and deepen understanding of the molecular mechanisms underlying AN. This understanding will lay the groundwork for improvements in diagnosis and prognosis, as well as the development of individualized therapeutic strategies. Additionally, exploring gene interactions and their impact on the structure and function of the auditory system could yield valuable insights and inform the development of innovative treatment approaches in the future.

Ethical Considerations

Compliance with ethical guidelines

No ethical approval was required as this study is a review of previously published literature and involved no human or animal subjects.

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Authors' contributions

Conceptualization and drafting of the manuscript: Majid karimi; Critical revisions: Mohsen Ahadi; Literature selection: Mohammad Ajalloueyan; Refining the scientific content: Nader Saki; Organization and synthesis of key findings: Saeid Morovvati; Reviewing and improving the final manuscript before submission: Golshan Mirmomeni; Reading and approval of the final version of the manuscript: All authors.

Conflict of interest

The authors declared no conflicts of interest.

References

[1] Kaga K. Auditory nerve disease and auditory neuropathy spectrum disorders. Auris, Nasus, Larynx. 2016; 43(1):10-20. [DOI:10.1016/j.anl.2015.06.008] [PMID]

[2] Hood LJ. Evaluation and management of patients with auditory neuropathy spectrum disorder. Hearing hearing technology. Paper presented at: 2020 AG Bell Global Virtual Lsl Symposium. 2020 July 10; Washington, USA. [Link]

[3] Moser T, Starr A. Auditory neuropathy - neural and synaptic mechanisms. Nature Reviews. Neurology. 2016; 12(3):135-49. [DOI:10.1038/nrneurol.2016.10] [PMID]

[4] Yuvaraj P, Jayaram M. Audiological profile of adult persons with auditory neuropathy spectrum disorders. Journal of Audiology & Otology. 2016; 20(3):158. [DOI:10.7874/jao.2016.20.3.158] [PMID]

[5] Song M, Li J, Lan L, Xie L, Xiong F, Yu L, et al. Clinical characteristics of patients with unilateral auditory neuropathy. American Journal of Otolaryngology. 2021; 42(5):103143. [DOI:10.1016/j.amjoto.2021.103143] [PMID]

[6] Almishaal AA, Saleh S, Alferaih H, Alhelo O. Prevalence, risk factors, and audiological characteristics of auditory neuropathy. International Journal of Audiology. 2022; 61(12):1018-26. [DOI:10.1080/14992027.2021.2014074] [PMID]

[7] Mittal R, Ramesh AV, Panwar SS, Nilkanthan A, Nair S, Mehra PR. Auditory neuropathy spectrum disorder: Its prevalence and audiological characteristics in an Indian tertiary care hospital. International Journal of Pediatric Otorhinolaryngology. 2012; 76(9):1351-4. [DOI:10.1016/j.ijporl.2012.06.005] [PMID]

[8] Penido RC, Isaac ML. Prevalence of auditory neuropathy spectrum disorder in an auditory health care service. Brazilian Journal of Otorhinolaryngology. 2013; 79(4):429-33. [DOI:10.5935/1808-8694.20130077] [PMID]

[9] Rajput K, Saeed M, Ahmed J, Chung M, Munro C, Patel S, et al. Findings from aetiological investigation of Auditory Neuropathy Spectrum Disorder in children referred to cochlear implant programs. International Journal of Pediatric Otorhinolaryngology. 2019; 116:79-83. [DOI:10.1016/j.ijporl.2018.10.010] [PMID]

[10] Manchaiah VKC, Zhao F, Danesh AA, Duprey R. The genetic basis of auditory neuropathy spectrum disorder (ANSD). International Journal of Pediatric Otorhinolaryngology. 2011; 75(2):151-8. [DOI:10.1016/j.ijporl.2010.11.023] [PMID]

[11] Sathasivam S. Brown-Vialetto-Van Laere syndrome. Orphanet Journal of Rare Diseases. 2008; 3(1):9. [DOI:10.1186/1750-1172-3-9] [PMID]

[12] Bamaga AK, Maamari RN, Culican SM, Shinawi M, Golumbek PT. Child neurology: Brown-vialetto-van laere syndrome. Neurology. 2018; 91(20):938-41. [DOI:10.1212/WNL.0000000000006498] [PMID]

[13] Woodcock IR, Menezes MP, Coleman L, Yaplito-Lee J, Peters H, White SM, et al. Genetic, radiologic, and clinical variability in brown-vialetto-van laere syndrome. Seminars in Pediatric Neurology. 2018; 26:2-9. [DOI:10.1016/j.spen.2017.03.001] [PMID]

[14] Chandran R, Alexander M, Naina P, Balraj A. Auditory neuropathy spectrum disorder with Brown-Vialetto-Van Laere syndrome: Challenges in hearing rehabilitation. The Journal of Laryngology and Otology. 2015; 129(5):504-8. [DOI:10.1017/S0022215114003375] [PMID]

[15] Reilly MM, Murphy SM, Laurá M. Charcot-Marie-Tooth disease. Journal of the Peripheral Nervous System. 2011; 16(1):1-14. [DOI:10.1111/j.1529-8027.2011.00324.x] [PMID]

[16] Mathis S, Goizet C, Tazir M, Magdelaine C, Lia AS, Magy L, et al. Charcot-marie-tooth diseases: An update and some new proposals for the classification. Journal of Medical Genetics. 2015; 52(10):681-90. [DOI:10.1136/jmedgenet-2015-103272] [PMID]

[17] Estévez-Arias B, Carrera-García L, Nascimento A, Cantarero L, Hoenicka J, Palau F. Genetic approaches and pathogenic pathways in the clinical management of charcot-marie-tooth disease. Journal of Translational Genetics and Genomics. 2022; 6:333-52. [DOI:10.20517/jtgg.2022.04]

[18] Giuliani N, Holte L, Shy M, Grider T. The audiologic profile of patients with charcot-marie tooth neuropathy can be characterised by both cochlear and neural deficits. International Journal of Audiology. 2019; 58(12):902-12. [DOI:10.1080/14992027.2019.1633022] [PMID]

[19] Pérez H, Vílchez J, Sevilla T, Martínez L. Audiologic evaluation in charcot-marie-tooth disease. Scandinavian Audiology. Supplementum. 1988; 30:211-3. [PMID]

[20] Sivera R, Cavalle L, Vílchez JJ, Espinós C, Pérez-Garrigues H, Sevilla T. Audiological findings in charcot-marie-tooth disease type 4C. The Journal of International Advanced Otology. 2017; 13(1):93-9. [DOI:10.5152/iao.2017.3379] [PMID]

[21] Pandolfo M. Friedreich ataxia. Archives of Neurology. 2008; 65(10):1296-303. [DOI:10.1001/archneur.65.10.1296] [PMID]

[22] Delatycki MB. Friedreich ataxia: An overview. Journal of Medical Genetics . 2000; 37(1):1-8. [DOI:10.1136/jmg.37.1.1] [PMID]

[23] Krasilnikova MM, Humphries CL, Shinsky EM. Friedreich's ataxia: New insights. Emerging Topics in Life Sciences. 2023; 7(3):313-23. [DOI:10.1042/ETLS20230017] [PMID]

[24] Rance G, Corben L, Barker E, Carew P, Chisari D, Rogers M, et al. Auditory perception in individuals with friedreich's ataxia. Audiology and Neurotology. 2010; 15(4):229-40. [DOI:10.1159/000255341] [PMID]

[25] Koohi N, Thomas-Black G, Giunti P, Bamiou DE. Auditory phenotypic variability in friedreich's ataxia patients. Cerebellum. 2021; 20(4):497-508. [DOI:10.1007/s12311-021-01236-9] [PMID]

[26] Zong L, Guan J, Ealy M, Zhang Q, Wang D, Wang H, et al. Mutations in apoptosis-inducing factor cause X-linked recessive auditory neuropathy spectrum disorder. Journal of Medical Genetics. 2015; 52(8):523-31. [DOI:10.1136/jmedgenet-2014-102961] [PMID]

[27] Rinaldi C, Grunseich C, Sevrioukova IF, Schindler A, Horkayne-Szakaly I, Lamperti C, et al. Cowchock syndrome is associated with a mutation in apoptosis-inducing factor. American Journal of Human Genetics. 2012; 91(6):1095-102. [DOI:10.1016/j.ajhg.2012.10.008] [PMID]

[28] Diodato D, Tasca G, Verrigni D, D'Amico A, Rizza T, Tozzi G, et al. A novel AIFM1 mutation expands the phenotype to an infantile motor neuron disease. European Journal of Human Genetics. 2016; 24(3):463-6. [DOI:10.1038/ejhg.2015.141] [PMID]

[29] Hardelin JP, Dodé C. The Complex Genetics of Kallmann Syndrome: KAL1, FGFR1, FGF8, PROKR2, PROK2, et al. Sexual Development. 2008; 2(4-5):181-93. [DOI:10.1159/000152034] [PMID]

[30] Salama N. Kallmann syndrome and deafness: An uncommon combination: A case report and a literature review. International Journal of Reproductive Biomedicine. 2016; 14(8):541-4. [DOI:10.29252/ijrm.14.8.541] [PMID]

[31] Marlin S, Chantot-Bastaraud S, David A, Loundon N, Jonard L, Portnoï MF, et al. Discovery of a large deletion of KAL1 in 2 deaf brothers. Otology & Neurotology. 2013; 34(9):1590-4. [DOI:10.1097/MAO.0000000000000228] [PMID]

[32] Hill J, Elliott C, Colquhoun I. Audiological, vestibular and radiological abnormalities in Kallman's syndrome. The Journal of Laryngology and Otology. 1992; 106(6):530-4. [DOI:10.1017/S0022215100120067] [PMID]

[33] Zentner GE, Layman WS, Martin DM, Scacheri PC. Molecular and phenotypic aspects of CHD7 mutation in CHARGE syndrome. American Journal of Medical Genetics. Part A. 2010; 152A(3):674-86. [DOI:10.1002/ajmg.a.33323] [PMID]

[34] Sanlaville D, Verloes A. CHARGE syndrome: An update. European Journal of Human Genetics. 2007; 15(4):389-99. [DOI:10.1038/sj.ejhg.5201778] [PMID]

[35] Hsu P, Ma A, Wilson M, Williams G, Curotta J, Munns CF, et al. CHARGE syndrome: A review. Journal of Paediatrics and Child Health. 2014; 50(7):504-11. [DOI:10.1111/jpc.12497] [PMID]

[36] Birman CS, Brew JA, Gibson WPR, Elliott EJ. CHARGE syndrome and Cochlear implantation: Difficulties and outcomes in the paediatric population. International Journal of Pediatric Otorhinolaryngology. 2015; 79(4):487-92. [DOI:10.1016/j.ijporl.2015.01.004] [PMID]

[37] Cole TRP. Sotos Syndrome. In: Cassidy SB, Allanson JE, editors. Management of genetic syndromes. Hoboken: Wiley; 2010. [DOI:10.1002/9780470893159.ch51]

[38] Baujat G, Cormier-Daire V. Sotos syndrome. Orphanet Journal of Rare Diseases. 2007; 2(1):36. [DOI:10.1186/1750-1172-2-36] [PMID]

[39] Gaudreau P, Zizak V, Gallagher TQ. The otolaryngologic manifestations of Sotos syndrome. International Journal of Pediatric Otorhinolaryngology. 2013; 77(11):1861-3. [DOI:10.1016/j.ijporl.2013.08.029] [PMID]

[40] Duat Rodriguez A, Prochazkova M, Santos Santos S, Rubio Cabezas O, Cantarin Extremera V, Gonzalez-Gutierrez-Solana L. Early diagnosis of capos syndrome before acute-onset ataxia-review of the literature and a new family. Pediatric Neurology. 2017; 71:60-4. [DOI:10.1016/j.pediatrneurol.2017.01.009] [PMID]

[41] Gao Y, Li F, Luo R, Chen G, Li D, Wang D, et al. [Clinical features of CAPOS syndrome caused by maternal ATP1A3 gene variation: A case report (Chinese)]. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2024; 38(1):73-6. [PMID]

[42] Atilgan A, Yuksel M, Ciprut A. Cochlear implantation in a case of auditory neuropathy spectrum disorder with CAPOS syndrome. Medeniyet Medical Journal. 2019; 34(3):318-3. [DOI:10.5222/MMJ.2019.53503] [PMID]

[43] Tranebjærg L, Strenzke N, Lindholm S, Rendtorff ND, Poulsen H, Khandelia H, et al. The CAPOS mutation in ATP1A3 alters Na/K-ATPase function and results in auditory neuropathy, which has implications for management. Human Genetics. 2018; 137(2):111-27. [DOI:10.1007/s00439-017-1862-z] [PMID]

[44] Varga R, Kelley PM, Keats BJ, Starr A, Leal SM, Cohn E, et al. Nonsyndromic recessive auditory neuropathy is the result of mutations in the otoferlin (OTOF) gene. Journal of Medical Genetics. 2003; 40(1):45-50. [DOI:10.1136/jmg.40.1.45] [PMID]

[45] Chiu YH, Wu CC, Lu YC, Chen PJ, Lee WY, Liu AYZ, et al. Mutations in the OTOF Gene in Taiwanese Patients with Auditory Neuropathy. Audiology and Neurotology. 2010; 15(6):364-74. [DOI:10.1159/000293992] [PMID]

[46] Romanos J, Kimura L, Fávero ML, Izarra FAR, de Mello Auricchio MTB, Batissoco AC, et al. Novel OTOF mutations in Brazilian patients with auditory neuropathy. Journal of Human Genetics. 2009; 54(7):382-5. [DOI:10.1038/jhg.2009.45] [PMID]

[47] Zadro C, Ciorba A, Fabris A, Morgutti M, Trevisi P, Gasparini P, et al. Five new OTOF gene mutations and auditory neuropathy. International Journal of Pediatric Otorhinolaryngology. 2010; 74(5):494-8. [DOI:10.1016/j.ijporl.2010.02.004] [PMID]

[48] Mahdieh N, Shirkavand A, Rabbani B, Tekin M, Akbari B, Akbari MT, et al. Screening of OTOF mutations in Iran: A novel mutation and review. International Journal of Pediatric Otorhinolaryngology. 2012; 76(11):1610-5. [DOI:10.1016/j.ijporl.2012.07.030] [PMID]

[49] Mujtaba G, Bukhari I, Fatima A, Naz S. A p.C343S missense mutation in PJVK causes progressive hearing loss. Gene. 2012; 504(1):98-101. [DOI:10.1016/j.gene.2012.05.013] [PMID]

[50] Zhang QJ, Lan L, Li N, Qi Y, Zong L, Shi W, et al. Identification of a novel mutation of PJVK in the Chinese nonsyndromic hearing loss population with low prevalence of the PJVK mutations. Acta Oto-Laryngologica. 2015; 135(3):211-6. [DOI:10.3109/00016489.2014.985799] [PMID]

[51] Domínguez-Ruiz M, Rodríguez-Ballesteros M, Gandía M, Gómez-Rosas E, Villamar M, Scimemi P, et al. novel pathogenic variants in PJVK, the gene encoding pejvakin, in subjects with autosomal recessive nonsyndromic hearing impairment and auditory neuropathy spectrum disorder. Genes. 2022; 13(1):149. [DOI:10.3390/genes13010149] [PMID]

[52] Nakanishi H, Kurima K, Kawashima Y, Griffith AJ. Mutations of TMC1 cause deafness by disrupting mechanoelectrical transduction. Auris, Nasus, Larynx. 2014; 41(5):399-408. [DOI:10.1016/j.anl.2014.04.001] [PMID]

[53] Kalay E, Karaguzel A, Caylan R, Heister A, Cremers FPM, Cremers CWRJ, et al. Four novelTMC1 (DFNB7/DFNB11) mutations in Turkish patients with congenital autosomal recessive nonsyndromic hearing loss. Human Mutation. 2005; 26(6):591. [DOI:10.1002/humu.9384] [PMID]

[54] Imtiaz A, Maqsood A, Rehman AU, Morell RJ, Holt JR, Friedman TB, et al. Recessive mutations of TMC1 associated with moderate to severe hearing loss. Neurogenetics. 2016; 17(2):115-23. [DOI:10.1007/s10048-016-0477-1] [PMID]

[55] Schoen CJ, Emery SB, Thorne MC, Ammana HR, Śliwerska E, Arnett J, et al. Increased activity of Diaphanous homolog 3 (DIAPH3)/diaphanous causes hearing defects in humans with auditory neuropathy and in Drosophila. Proceedings of the National Academy of Sciences. 2010; 107(30):13396-401. [DOI:10.1073/pnas.1003027107] [PMID]

[56] Wu K, Wang H, Guan J, Lan L, Zhao C, Zhang M, et al. A novel variant in diaphanous homolog 1 (DIAPH1) as the cause of auditory neuropathy in a Chinese family. International Journal of Pediatric Otorhinolaryngology. 2020; 133:109947. [DOI:10.1016/j.ijporl.2020.109947] [PMID]

[57] Leruez S, Milea D, Defoort-Dhellemmes S, Colin E, Crochet M, Procaccio V, et al. Sensorineural hearing loss in OPA1-linked disorders. Brain. 2013; 136(7):e236. [DOI:10.1093/brain/aws340] [PMID]

[58] Affortit C, Coyat C, Saidia AR, Ceccato JC, Charif M, Sarzi E, et al. The human OPA1delTTAG mutation induces adult onset and progressive auditory neuropathy in mice. Cellular and Molecular Life Sciences. 2024; 81(1):80. [DOI:10.1007/s00018-024-05115-4] [PMID]

[59] Huang T, Santarelli R, Starr A. Mutation of OPA1 gene causes deafness by affecting function of auditory nerve terminals. Brain Research. 2009; 1300:97-104. [DOI:10.1016/j.brainres.2009.08.083] [PMID]

[60] Lang-Roth R, Fischer-Krall E, Kornblum C, Nürnberg G, Meschede D, Goebel I, et al. AUNA2: A novel type of nonsyndromic slowly progressive auditory synaptopathy/auditory neuropathy with autosomal-dominant inheritance. Audiology and Neurotology. 2017; 22(1):30-40. [DOI:10.1159/000474929] [PMID]

[61] Liu Y, Ke X, Qi Y, Li W, Zhu P. Connexin26 gene (GJB2): Prevalence of mutations in the Chinese population. Journal of Human Genetics. 2002; 47(12):0688-90. [DOI:10.1007/s100380200106] [PMID]

[62] Iossa S, Marciano E, Franze A. GJB2 gene mutations in syndromic skin diseases with sensorineural hearing loss. Current Genomics. 2011; 12(7):475-85. [DOI:10.2174/138920211797904098] [PMID]

[63] de Carvalho GM, Z. Ramos P, M. Castilho A, C. Guimarães A, L. Sartorato E. Relationship between patients with clinical auditory neuropathy spectrum disorder and mutations in Gjb2 Gene. The Open Neurology Journal. 2016; 10(1):127-35. [DOI:10.2174/1874205X01610010127] [PMID]

[64] Li Y, Wang H, Li D, Wang Q. [Distribution characteristics and correlation analysis of GJB2 variation in patients with auditory neuropathy (Chinese)]. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2024; 38(1):23-9. [PMID]

[65] Saidia AR, Ruel J, Bahloul A, Chaix B, Venail F, Wang J. Current advances in gene therapies of genetic auditory neuropathy spectrum disorder. Journal of Clinical Medicine. 2023; 12(3):738. [DOI:10.3390/jcm12030738] [PMID]

[66] De Siati RD, Rosenzweig F, Gersdorff G, Gregoire A, Rombaux P, Deggouj N. Auditory neuropathy spectrum disorders: From diagnosis to treatment: Literature review and case reports. Journal of Clinical Medicine. 2020; 9(4):1074. [DOI:10.3390/jcm9041074] [PMID]