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A Case Report of Norrie Disease with Congenital Sensorineural Hearing Loss

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Case Report

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Abstract

Norrie Disease (ND) is a rare X-linked recessive genetic disorder caused by mutations in the Norrie disease protein (NDP) gene on the X chromosome. This disorder leads to congenital or neonatal blindness, progressive hearing loss in adolescence, and cognitive or behavioral problems. Although hearing loss is a characteristic feature of ND, it is often overlooked due to the prominence of ocular symptoms. This article presents a rare case of ND in a 3-month-old boy who failed the universal newborn hearing screening (UNHS) bilaterally, further audiological evaluation revealed bilateral sensorineural hearing loss. Suggests that patients with ND may be born with congenital hearing loss, earlier than the previous reports. Addressing hearing loss at an early stage can help minimize the compounding effect on cognitive functioning and improve overall mental well-being.

Keywords: Norrie Disease; Audiological; ND Patients

Introduction

Norrie Disease (ND) is a rare genetic disorder that is X-linked recessive. Norrie disease protein (NDP) gene mutation located on the short arm of the X chromosome (Xp11.3) leads to defective norrin [1,2]. ND patients will have a classic triad of blindness from birth or as neonates, progressive hearing loss in adolescence, and cognitive or behavioral problems. Previous reports from cross-sectional studies indicate a progressive decline in hearing sensitivity [2,3].

Case Presentation

A 3-month-old boy was referred to our department of ENT for further audiological evaluation and treatment, from the specialist pediatric ophthalmology clinic with left corneal opacification history and right tractional retinal detachment. Physical examination and history revealed that he failed the universal newborn hearing screening (UNHS) bilaterally, and he has a history of premature delivery, developmental delay, hypothyroidism, and anemia. Genetic testing was performed, and the clinical diagnosis is Norrie Disease. Further audiological diagnosis showed that sensorineural hearing loss bilaterally, the auditory nerve brainstem evoked response (ABR) thresholds for air conduction are as follows: 50 dB nHL for the left ear and 50 dB nHL for the right ear, and the bone conduction are as follows: 40 dB nHL for the left ear and 50 dB nHL for the right ear. The types of the tympanometric curve were type-As for the left ear and B for the right ear. Additionally, there were absent Distortion Product Otoacoustic Emissions (DPOAE) bilaterally.

Discussion

Norrie disease (ND) is a condition that leads to congenital or neonatal bilateral blindness due to the abnormal development and detachment of the retina [4]. Ophthalmologic manifestations represent the initial and earliest signs of ND in male children and are nearly ubiquitous in affected individuals. Additionally, ND is characterized by extraocular phenotypes, which include sensorineural hearing loss, cognitive impairment, behavioral disturbances, seizures, and peripheral vascular disease [5,6]. The onset and progression of hearing loss in individuals with ND exhibit different characteristics compared to the early appearance of the typical ocular symptoms. While both ocular symptoms and hearing loss are characteristic features of ND, the onset and manifestation of hearing loss seem to occur later in life compared to the early appearance of ocular symptoms [7].

According to reports, almost all ND patients will develop some level of hearing loss over the course of their lives. Tinnitus or a sense of stuffiness in the ears are frequently the first signs of hearing loss in people with ND. The hearing loss typically worsens as affected people become older, and severe bilateral deafness is possible. Notably, people with ND normally have normal hearing at birth, although hearing loss can start as early as 5 years old or happen as late as 48 years old [8]. In this case, the patient did not pass the hearing screening at birth, and the hearing loss was detected during an audiological diagnosis at 3 months of age. This finding suggests that ND might directly contribute to congenital hearing loss, which occurs earlier than the previously reported hearing loss observed during adolescence or adulthood [7,9].

The diagnosis of ND is often a time-consuming process. Initial ophthalmic assessment involves the observation of characteristic symptoms such as nystagmus (rapid, involuntary eye movements), leukocoria (abnormal white reflection from the retina), or failure of the infant to fix their gaze and follow movement. Due to the rarity of the condition, appropriate referral and diagnosis may be postponed, increasing the risk of misdiagnosis for conditions including glaucoma, congenital cataract, or retinoblastoma [9]. Most patients will eventually be referred to a specialist pediatric ophthalmologist, who will conduct a comprehensive examination and investigations, including B-mode ultrasound and subsequent genetic testing, and get finally diagnosed. At this point, there is often a delay and neglect in the diagnosis of the hearing impairment.

The progressive deterioration of sensory function in patients with ND becomes increasingly challenging as they heavily rely on their remaining hearing abilities due to the lack of visual input. According to findings from clinical studies, the impairment of auditory function initially targets high-frequency sounds, resulting in typically mild and asymmetric hearing loss [7-10]. The assessment of auditory brainstem response (ABR) thresholds in ND patients reveals a distinct pattern described as “skewed” or “boat-shaped.” This pattern indicates that specific frequency-specific sites in the auditory system are more heavily affected than others [7,9]. In a study involving three patients with ND in their 30s, normal hair cell, and auditory brainstem function were observed. However, further investigation revealed a cochlear lesion at the level of the spiral ganglion neurons (SGN) and the auditory nerve, as indicated by abnormal whole-nerve action potential [11]. On the other hand, some researchers have put forward the hypothesis that certain patient-reported symptoms, such as “stuffiness” at the onset of hearing loss, tinnitus, and temporary, fluctuating, intermittent hearing loss, could be indicative of temporary abnormalities in the composition of the endolymphatic fluid at the early stages of the disease. These abnormalities might lead to disruptions in the endocochlear potential (EP) or result in endolymphatic hydrops, which is characterized by the ballooning of the endolymph fluid in the inner ear [7,12-14].

In most cases, the use of hearing aids has been demonstrated to be effective in managing hearing loss in individuals with ND throughout their middle or late adulthood. For individuals with more severe hearing loss, where hearing aids may not provide sufficient benefit, cochlear implants can be considered as an alternative option [15]. Individuals with ND and hearing impairment need to work closely with audiologists and healthcare professionals to determine the most suitable intervention to optimize their hearing abilities and improve their quality of life. Regular follow-up and adjustments to hearing devices are also important to ensure continued effectiveness.

Indeed, developmental delay or cognitive impairment is a significant concern for individuals with ND. The cognitive and developmental deficits resulting from hearing loss in individuals with ND can have a compounding effect on their overall cognitive functioning. Hearing loss can hinder the acquisition of language and communication skills during critical developmental periods, which may exacerbate cognitive deficits already present in ND patients. Moreover, the challenges in communication and social interaction may contribute to feelings of loneliness and depression in ND patients with hearing loss. Depression can further impact cognitive function and overall mental well-being, creating a complex interplay between cognitive deficits, hearing impairment, and psychological health.

Conclusion

ND is a rare genetic disorder and contributes to multisensory impairment, Hearing loss is often ignored

because of ocular symptoms. Newborn hearing screening and early diagnosis of hearing loss can lead to early detection and intervention, further reducing the cognitive and developmental impact of hearing loss. Early detection, prompt treatment, and hearing compensation can help improve outcomes for patients with ND. Close monitoring and follow-up care are essential to manage potential complications and optimize the quality of life for affected individuals.

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